

=> fil uspat; s wang, yi?/in; s matis, louis?/in; s rollins, scott?/in
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* WELCOME TO THE *
* U. S. PATENT TEXT FILE *

L1 36 WANG, YI?/IN

A + B → C

L2 1 MATIS, LOUIS?/IN

L3 1 ROLLINS, SCOTT?/IN

=> s (c5 or c5a or c5b or complement?); s (l1 or l2 or l3) and l4

10781 C5

201 C5A

58 C5B

131552 COMPLEMENT?

L4 140707 (C5 OR C5A OR C5B OR COMPLEMENT?)

L5 3 (L1 OR L2 OR L3) AND L4

=> d 1-3 .bevpat; s l4 and (glomerulonephr? or nephrit? or diabet? or immun?(w)complex?)

US PAT NO: 5,329,025 [IMAGE AVAILABLE]

L5: 1 of 3

DATE ISSUED: Jul. 12, 1994

INVENTOR: Chi-Huey Wong, College Station, TX

Richard L. Pederson, College Station, TX

Yi-Fong Wang, College Station, TX

SEARCH-FLD: 435/122; 548/960; 534/550; 552/1, 10; 568/423

ABSTRACT:

A new and practical method for synthesizing heterocyclic polyhydroxylated alkaloids using enzymatic aldol condensation and catalytic intramolecular reductive amination is disclosed.

US PAT NO: 5,226,747 [IMAGE AVAILABLE]

L5: 2 of 3

DATE ISSUED: Jul. 13, 1993

INVENTOR: **Yichang Wang**, Tianjin, China

Shaohong Chen, Tianjin, China

Chengdong Mu, Tianjin, China

Hong Shi, Tianjin, China

Hui Chen, Tianjin, China

Jianping Yuan, Tianjin, China

SEARCH-FLD: 405/52, 79, 80; 4/491, 492

ABSTRACT:

An adaptive control artificial wavemaking device comprises an air blower as shock wave source. According to the invention, the device further

comprises a control system consisted of a float, a sensor, a control circuit and electromagnetic actuators; butterfly valves; and air chamber for generating shock wave. When the sensor receives signals from the float, the signals are transferred through the control circuit to actuate the electromagnetic actuators to control opening and closing of said butterfly valves to enable the air chamber to generate a shock wave which is in resonance with the water wave. The device may further comprises an oscillator for generating shock wave of a given frequency during starting. The device according to the invention has the advantage of simplified structure, low manufacture cost and low energy consumption, thus it may be widely used for aquatic breeding, sport, recreation and medical facilities.

US PAT NO: 5,106,750 [IMAGE AVAILABLE]

L5: 3 of 3

DATE ISSUED: Apr. 21, 1992

INVENTOR: Chi-Huey Wong, College Station, TX
Yi-Fong Wang, College Station, TX
William J. Hennen, Bryan, TX
Kevin A. Babiak, Evanston, IL
John H. Dygos, Northbrook, IL
John S. Ng, Chicago, IL

SEARCH-FLD: 435/280, 135, 134

ABSTRACT:

A process for irreversible regio- and stereoselective enzyme catalyzed acylation of alcohols using enol esters as acylating reagents is disclosed. The present invention permits the selective modification of hydroxyl group(s) of chiral and meso alcohols, including sugars, organometallics, and glycosides. The enol freed upon transesterification rapidly tautomerizes to the corresponding volatile aldehyde or ketone thereby preventing the reverse reaction from occurring.

580 GLOMERULONEPHR?
695 NEPHRIT?
6079 DIABET?
34894 IMMUN?
287092 COMPLEX?
1497 IMMUN?(W) COMPLEX?

L6 1302 L4 AND (GLOMERULONEPHR? OR NEPHRIT? OR DIABET? OR IMMUN?(W)
COM PLEX?)

=> s 16 and (treat? or therap?)
429765 TREAT?

L7 53944 THERAP?
1217 L6 AND (TREAT? OR THERAP?)

=> s 17 and antibod?
15888 ANTIBOD?

L8 967 L7 AND ANTIBOD?

=> s 18 and (blood? or plasma)
71787 BLOOD?

D ← B + glomerul?

49381 PLASMA
 L9 882 L8 AND (BLOOD? OR PLASMA)
 => s l9 and (bind? or bound?); s l10 not l5
 159048 BIND?
 191505 BOUND?
 L10 807 L9 AND (BIND? OR BOUND?)

 L11 807 L10 NOT L5
 => s l11 and (method# or technique# or admin? or dos?)
 934000 METHOD#
 448395 TECHNIQUE#
 76195 ADMIN?
 96881 DOS?
 L12 806 L11 AND (METHOD# OR TECHNIQUE# OR ADMIN? OR DOS?)
 => s l12 and (cell#(3a)lys?)
 TERM 'LYS?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED
 => s l12 and (cell#(3a)(lysis or lyse or lysing))
 177958 CELL#
 3910 LYSIS
 1319 LYSE
 1530 LYSING
 2436 CELL#(3A)(LYSIS OR LYSE OR LYSING)
 L13 162 L12 AND (CELL#(3A)(LYSIS OR LYSE OR LYSING))
 => s l12 and (cell#(3a)lysed); s l13 or l14
 177958 CELL#
 3078 LYSED
 1588 CELL#(3A)LYSED
 L14 98 L12 AND (CELL#(3A)LYSED)

 L15 203 L13 OR L14
 => s l15 and pharmac?
 76044 PHARMAC?
 L16 156 L15 AND PHARMAC?
 => s l16 and (monoclon? or mab# or moab#)
 5761 MONOCLON?
 1165 MAB#
 112 MOAB#
 L17 120 L16 AND (MONOCLON? OR MAB# OR MOAB#)
 => s l17 and c3b
 209 C3B
 L18 17 L17 AND C3B
 => s l17 not l18

L19 103 L17 NOT L18

=> d l18 1-17 .bevpat; d l19 1-103; s (antic5 or anti(w)c5)(1)antibod?
US PAT NO: 5,348,876 [IMAGE AVAILABLE] L18: 1 of 17
DATE ISSUED: Sep. 20, 1994
INVENTOR: Terje Michaelson, Hagan, Norway
Inger Sandlie, Oslo, Norway
SEARCH-FLD: 530/387.3; 435/69.6, 69.7, 172.3, 240.2, 320.1; 536/23.53

ABSTRACT:

The present invention provides modified IgG3 containing human constant regions which has a shorter total-hinge region compared with normal human IgG3. Also described is a ****method**** for assaying an ****antibody**** against a specific antigen or hapten for its effectiveness in ****complement**** activation in an animal species, wherein the ****antibody**** is contacted with the immobilized antigen or hapten to form an immobilized ****antibody**/antigen or hapten complex** which is then contacted with ****complement**** from the relevant animal species, followed by assay of components of the ****complement**** complex thereby formed; whereby the extent and nature of ****complement**** activation by the ****antibody**** in the sample may be determined.

US PAT NO: 5,334,584 [IMAGE AVAILABLE] L18: 2 of 17
DATE ISSUED: Aug. 2, 1994
INVENTOR: Randal W. Scott, Cupertino, CA
Marian N. Marra, San Mateo, CA
SEARCH-FLD: 514/12, 21

ABSTRACT:

The present invention provides a ****method**** for preventing endotoxin-associated shock in a subject which comprises ****administering**** to the subject an amount of a BPI protein effective to ****bind**** to endotoxin so as to prevent endotoxin associated shock in the subject. This invention further provides a ****method**** for ****treating**** a subject suffering from endotoxin-associated shock which comprises ****administering**** to the subject an amount of a BPI protein effective to ****bind**** endotoxin so as to ****treat**** the subject suffering from endotoxin-associated shock.

US PAT NO: 5,308,834 [IMAGE AVAILABLE] L18: 3 of 17
DATE ISSUED: May 3, 1994
INVENTOR: Randal W. Scott, Cupertino, CA
Marian N. Marra, San Mateo, CA
SEARCH-FLD: 514/12, 8, 21

ABSTRACT:

The present invention provides a ****method**** for preventing endotoxin-associated shock in a subject which comprises ****administering**** to the subject an amount of a BPI protein effective to ****bind**** to endotoxin so as to prevent endotoxin associated shock in the subject. This invention further provides a ****method**** for ****treating**** a subject suffering from endotoxin-associated shock which comprises ****administering**** to the subject an amount of a BPI protein effective to ****bind**** endotoxin so as to ****treat**** the subject suffering from

endotoxin-associated shock.

US PAT NO: 5,264,357 [IMAGE AVAILABLE] L18: 4 of 17
DATE ISSUED: Nov. 23, 1993
INVENTOR: Ingrid W. Caras, San Francisco, CA
Michael A. Davitz, Riverdale, NY
Victor Nussenzweig, New York, NY
David W. Martin, Jr., San Francisco, CA
SEARCH-FLD: 536/27, 23.4; 435/320.1, 240.1, 240.2, 252.3, 69.7

ABSTRACT:

Novel fusions of a phospholipid anchor domain and a polypeptide heterologous to the anchor domain donor polypeptide are provided for industrial use. ****Therapeutic**** ****administration**** of the fusions enables the targeting of biological activity to cell membrane surfaces.

US PAT NO: 5,256,642 [IMAGE AVAILABLE] L18: 5 of 17
DATE ISSUED: Oct. 26, 1993
INVENTOR: Douglas T. Fearon, Baltimore, MD
Lloyd B. Klickstein, Brookline, MA
Winnie W. Wong, Newton, MA
Gerald R. Carson, Wellesley, MA
Michael F. Concino, Newton, MA
Stephen H. Ip, Sudbury, MA
Savvas; C. Makrides, Bedford, MA
Henry C. Marsh, Jr., Reading, MA
SEARCH-FLD: 424/94.63, 94.64; 514/2, 8; 435/215, 216; 530/350

ABSTRACT:

The present invention relates to compositions comprising soluble ****complement**** receptor 1 (CR1) and a thrombolytic agent. In a specific embodiment, the thrombolytic agent is anisoylated human plasminogen-streptokinase activator complex (ASPAC). The invention further relates to ****methods**** for ****treating**** thrombotic conditions in humans and animals by ****administering**** a composition comprising soluble CR1 and a thrombolytic agent. In particular, the compositions and ****methods**** are useful both for reducing reperfusion injury and ameliorating the other effects of myocardial infarction.

US PAT NO: 5,238,839 [IMAGE AVAILABLE] L18: 6 of 17
DATE ISSUED: Aug. 24, 1993
INVENTOR: Harvey I. Cantor, Wellesley, MA
Roberto Patarca, Brookline, MA
Joel L. Schwartz, Newton Centre, MA
Gordon Freeman, Brookline, MA
SEARCH-FLD: 435/320.1, 252.33, 256, 240.1, 240.2, 240.2, 252.3, 255;
536/27, 23.5

ABSTRACT:

The present invention relates to genes and their encoded proteins which induce immunological effector cell activation and chemattraction. The proteins of the invention attract subsets of immunological effector cells and stimulate them to express their specialized effector cell functions. Such proteins, termed Ap-1 proteins, are expressed by lymphoid cells, and ****bind**** to effector cells such as macrophages and mast cells. In particular, the Ap

Pursuant to the provisions of 35 U.S.C. .sctn.202(c), it is hereby acknowledged that the Government has certain rights in this invention, which was made in part with funds from the National Institutes of Health.

US PAT NO: 5,212,071 [IMAGE AVAILABLE] L18: 7 of 17

DATE ISSUED: May 18, 1993

INVENTOR: Douglas T. Fearon, Baltimore, MD
Lloyd B. Klickstein, Brookline, MA
Winnie W. Wong, Newton, MA
Gerald R. Carson, Wellesley, MA
Michael F. Concino, Newton, MA
Stephen H. Ip, Sudbury, MA
Savvas C. Makrides, Bedford, MA

SEARCH-FLD: 435/69.1, 172.3, 252.3, 320.1; 530/350; 536/27

US PAT NO: 5,173,499 [IMAGE AVAILABLE] L18: 8 of 17

DATE ISSUED: Dec. 22, 1992

INVENTOR: Robert D. Sindelar, Oxford, MS
Barton J. Bradbury, Columbia, MD
Teodoro Kaufman, University, MS
Stephen H. Ip, Framingham, MA
Henry C. Marsh, Jr., Watertown, MA

SEARCH-FLD: 549/345; 514/462, 825

ABSTRACT:

The present invention is directed to compounds which suppress immune responses and/or selectively inhibit ****complement****. These compounds contain an aromatic ring and are substituted dihydrobenzofurans, spirobenzofuran-2(3H)-cycloalkanes, and their open chain intermediates. The compounds of the present invention, and the ****pharmaceutically**** acceptable salts thereof, interrupt the proteolytic processing of ****C5**** to bioactive components, exhibit immunosuppressive activities, and have ****therapeutic**** utility in the amelioration of disease and disorders mediated by ****complement**** and/or immune activity.

US PAT NO: 5,171,739 [IMAGE AVAILABLE] L18: 9 of 17

DATE ISSUED: Dec. 15, 1992

INVENTOR: Randal W. Scott, Cupertino, CA
Marian N. Marra, San Mateo, CA

SEARCH-FLD: 514/12

ABSTRACT:

The present invention provides a ****method**** for preventing endotoxin-associated shock in a subject which comprises ****administering**** to the subject an amount of a BPI protein effective to ****bind**** to endotoxin so as to prevent endotoxin associated shock in the subject. This invention further provides a ****method**** for ****treating**** a subject suffering from endotoxin-associated shock which comprises ****administering**** to the subject an amount of a BPI protein effective to ****bind**** endotoxin so as to ****treat**** the subject suffering from endotoxin-associated shock.

US PAT NO: 5,156,840 [IMAGE AVAILABLE] L18: 10 of 17

DATE ISSUED: Oct. 20, 1992

INVENTOR: John W. F. Goers, Atascadero, CA
Hurley D. King, Yardley, PA

Chyi Lee, New Brunswick, NJ
Daniel J. Coughlin, Plainsboro, NJ
Vernon L. Alvarez, Morrisville, PA
John D. Rodwell, Yardley, PA
Thomas J. McKearn, New Hope, PA

SEARCH-FLD: 514/410; 424/85.91

ABSTRACT:

The invention relates to amine-containing porphyrin derivatives. The porphyrins can be used as photosensitizers which are useful as ****therapeutic**** agents. Also described are ****methods**** for preparing conjugates in which a porphyrin derivative is covalently attached to an ****antibody**** or ****antibody**** fragment. In vivo ****therapeutic**** ****methods**** utilizing the conjugates are also desired.

US PAT NO: 5,109,113 [IMAGE AVAILABLE] L18: 11 of 17

DATE ISSUED: Apr. 28, 1992

INVENTOR: Ingrid W. Caras, San Francisco, CA
Michael A. Davitz, Riverdale, NY
Victor Nussenzweig, New York, NY
David W. Martin, Jr., San Francisco, CA

SEARCH-FLD: 530/359, 350, 405, 409, 806, 807, 808; 435/69

ABSTRACT:

Novel fusions of a phospholipid anchor domain and a polypeptide heterologous to the anchor domain donor polypeptide are provided for industrial use. ****Therapeutic**** ****administration**** of the fusions enables the targeting of biological activity to cell membrane surfaces.

US PAT NO: 5,089,274 [IMAGE AVAILABLE] L18: 12 of 17

DATE ISSUED: Feb. 18, 1992

INVENTOR: Marian N. Marra, San Mateo, CA
Randal W. Scott, Sunnyvale, CA

SEARCH-FLD: 424/534; 512/2, 21; 530/829

ABSTRACT:

The present invention provides a ****method**** of inhibiting lipopolysaccharide (LPS)-mediated stimulation of cells. This ****method**** comprises contacting the cells, in the presence of a cell-stimulating amount of lipopolysaccharide, with Bactericidal/Permeability Increasing Protein (BPI) in an amount effective to inhibit cell stimulation.

US PAT NO: 5,049,659 [IMAGE AVAILABLE] L18: 13 of 17

DATE ISSUED: Sep. 17, 1991

INVENTOR: Harvey I. Cantor, Wellesley, MA
Roberto M. Patarca, Brookline, MA
Joel L. Schwartz, Newton Centre, MA

SEARCH-FLD: 530/350, 351; 424/85.1

ABSTRACT:

The present invention relates to genes and their encoded proteins which induce immunological effector cell activation and chemotaxis. The proteins of the invention attract subsets of immunological effector cells and stimulate them to express their specialized effector cell functions. Such proteins, termed Ap-1 proteins, are expressed by lymphoid cells, and ****bind**** to effector cells such as macrophages and mast cells. In

particular, the Ap-1 proteins induce macrophage phagocytosis, expression of class II major histocompatibility molecules, cytotoxicity, and migration, and induce hematopoietic progenitor cell differentiation. The Ap-1 molecules can be of value in the **therapy** or diagnosis of inflammatory or immune disorders, or neoplasia.

US PAT NO: 4,867,973 [IMAGE AVAILABLE] L18: 14 of 17

DATE ISSUED: Sep. 19, 1989

INVENTOR: John W. F. Goers, Atascadero, CA
Hurley D. King, Yardley, PA
Chyi Lee, New Brunswick, NJ
Daniel J. Coughlin, Plainsboro, NJ
Vernon L. Alvarez, Morrisville, PA
John D. Rodwell, Yardley, PA
Thomas J. McKearn, New Hope, PA

SEARCH-FLD: 530/387, 388, 389, 390, 391, 828; 514/2, 68; 424/85, 86,
87; 427/85.91, 85.8

ABSTRACT:

This invention relates to **antibody**--**therapeutic** agent conjugates having a **therapeutic** agent covalently attached to an **antibody** or **antibody** fragment. Also described are **methods** for intermediates in the preparation of **antibody** conjugates. **Therapeutic** in vivo **methods** utilizing such **antibody**--**therapeutic** agent conjugates are described.

US PAT NO: 4,699,783 [IMAGE AVAILABLE] L18: 15 of 17

DATE ISSUED: Oct. 13, 1987

INVENTOR: David S. Terman, 25371 Outlook Dr., Carmel, CA 93923
Joseph P. Balint, 169 Crooks Ave., Clifton, NJ 07011
John J. Langone, 7735 Candlegreen, Houston, TX 77071

SEARCH-FLD: 424/85, 101; 260/112R, 112B; 530/387

ABSTRACT:

Disclosed are compositions for the **treatment** of cancer, such as lymphomas and solid tumors, **methods** of producing these compositions, and **methods** and regimens in using these compositions in the **treatment** of hosts having cancer. The compositions are (1) tumor immune preparations which can be prepared by acidification or alkalization of an enriched immunoglobulin effluent from forced flow electrophoresis of **plasma** from a normal or a tumor bearing host, (2) tumor immune globulin which can be prepared by acidifying a Cohn gamma globulin fraction from a normal or a tumor bearing host, (3) protein A-IgG preparations which can be prepared by perfusion of **plasma** over protein A from staphylococcus aureus Cowans I and precipitating the complex or by incubating protein A and purified IgG or IgG in **plasma**, (4) tumor immune **plasma** preparations which may be prepared by acidification of **plasma** from normal or tumor bearing hosts, and (5) zymosan activated **plasma** which can be prepared by incubating **plasma** with zymosan and then removing the zymosan. Infusing of the compositions alone or in combination with each other and with various chemotherapeutic agents has resulted in tumoricidal reactions, objective anti-tumor effects, and sustained tumor regressions.

US PAT NO: 4,672,044 [IMAGE AVAILABLE] L18: 16 of 17

DATE ISSUED: Jun. 9, 1987

INVENTOR: Robert D. Schreiber, Encinitas, CA
SEARCH-FLD: 260/112.5R; 424/85, 177, 1.1; 435/4, 7, 68, 70, 172.2,
240, 948, 810; 436/504, 506, 507, 512, 518, 536-542,
548, 804, 815, 821, 823, 828, 810, 501; 935/93, 104,
110, 58-85; 530/387

ABSTRACT:

A murine ****monoclonal**** ****antibody**** combining site produced by a hybridoma formed by fusion of cells from a myeloma cell line and lymphocytes that produce ****antibodies**** that react (1) with isolated human ****C3b**** receptor and (2) with ****C3b**** receptor-bearing cells from a mammal immunized with human ****C3b**** receptor is disclosed.

US PAT NO: 4,642,284 [IMAGE AVAILABLE] L18: 17 of 17
DATE ISSUED: Feb. 10, 1987
INVENTOR: Neil Cooper, San Diego, CA
James T. Mayes, La Jolla, CA
SEARCH-FLD: 436/821, 540, 7, 512

ABSTRACT:

A ****method**** and system for detecting and preferably measuring the presence of an activated ****complement**** complex in a sample is discussed. The presence of such an activated complex is indicative of ****complement**** pathway activation and includes a first ****complement**** component and a second ****complement**** component. The ****method**** uses a first ****binding**** agent specific to the first ****complement**** component and a second ****binding**** agent specific to the second ****complement**** component which when ****bound**** with the complex forms an aggregate. The second specific ****binding**** agent includes a label whose presence is used to detect and measure the amount of aggregate and therefore activated complex in a sample. An assay system and aggregate for use in an assay system are also discussed.

1. 5,350,836, Sep. 27, 1994, Growth hormone antagonists; John J. Kopchick, et al., 530/399; 435/69.4 [IMAGE AVAILABLE]

2. 5,350,683, Sep. 27, 1994, DNA encoding type II interleukin-1 receptors; John E. Sims, et al., 435/69.1, 252.3, 320.1; 530/350; 536/23.5 [IMAGE AVAILABLE]

3. 5,346,989, Sep. 13, 1994, Peptides for use in induction of T cell activation against HIV-1; Anders Vahlne, et al., 530/324; 424/188.1, 208.1; 530/325 [IMAGE AVAILABLE]

4. 5,340,935, Aug. 23, 1994, DNAs encoding proteins active in lymphocyte-mediated cytotoxicity; Paul J. Anderson, et al., 536/23.5; 530/350; 536/24.31 [IMAGE AVAILABLE]

5. 5,336,491, Aug. 9, 1994, ****Methods**** and compositions for the ****treatment**** and diagnosis of shipping fever; Peter Berget, et al., 424/190.1, 255.1, 823; 435/69.1, 69.3, 71.1, 71.2; 530/350, 387.9, 388.4, 389.5; 536/23.7 [IMAGE AVAILABLE]

6. 5,330,896, Jul. 19, 1994, ****Monoclonal**** ****antibodies**** to an autocrine growth factor antigen that ****binds**** to activated lymphocytes and cancer cells; Ronald J. Billing, 435/7.23, 7.24, 7.8; 436/503, 518, 536, 813; 530/399, 403, 828 [IMAGE AVAILABLE]
7. 5,328,985, Jul. 12, 1994, Recombinant streptavidin-protein chimeras useful for conjugation of molecules in the immune system; Takeshi Sano, et al., 530/350; 435/7.1, 69.1, 252.3, 320.1; 530/391.1, 391.5; 536/22.1, 23.1, 23.2, 23.4, 23.7 [IMAGE AVAILABLE]
8. 5,324,820, Jun. 28, 1994, Acid-labile subunit (ALS) of insulin-like growth factor ****binding**** protein complex; Robert C. Baxter, 530/350; 435/69.1; 530/412, 413 [IMAGE AVAILABLE]
9. 5,324,510, Jun. 28, 1994, Use of ****antibodies**** to intercellular adhesion molecule-1 (ICAM-1) in the ****treatment**** of asthma; Craig D. Wegner, et al., 424/139.1, 152.1, 153.1, 154.1; 530/388.22, 388.7, 388.85, 389.6, 866, 868 [IMAGE AVAILABLE]
10. 5,322,769, Jun. 21, 1994, ****Methods**** for using CKS fusion proteins; Timothy J. Bolling, et al., 435/5, 7.1, 7.2, 7.92; 530/324, 327 [IMAGE AVAILABLE]
11. 5,321,127, Jun. 14, 1994, Antiplatelet and antithrombotic activity of platelet glycoprotein Ib receptor fragments; Robert Handin, 530/383; 435/69.6; 436/501; 530/380, 413 [IMAGE AVAILABLE]
12. 5,321,123, Jun. 14, 1994, Protein S polypeptides and anti-peptide ****antibodies**** that inhibit protein S ****binding**** to C4B ****binding**** protein, diagnostic systems and ****therapeutic**** ****methods****; John H. Griffin, et al., 530/300; 435/7.93; 436/501; 530/324, 325, 327, 328, 329, 830 [IMAGE AVAILABLE]
13. 5,314,813, May 24, 1994, Drosophila cell lines expressing genes encoding MHC class I antigens and B2-microglobulin and capable of assembling empty complexes and ****methods**** of making said cell lines; Per A. Peterson, et al., 435/172.3, 240.1, 320.1 [IMAGE AVAILABLE]
14. 5,308,838, May 3, 1994, Uses of aloe products; Bill H. McAnalley, et al., 424/278.1; 514/54, 885 [IMAGE AVAILABLE]
15. 5,306,614, Apr. 26, 1994, ****Methods**** and kits for diagnosing human immunodeficiency virus type 2(HIV-2); Marc Alizon, et al., 435/5, 7.1, 7.92, 7.93, 7.94, 7.95, 974; 530/300, 324, 325, 326, 350 [IMAGE AVAILABLE]
16. 5,302,384, Apr. 12, 1994, Endothelial-derived Il-8 Adhesion Inhibitor; Michael A. Gimbrone, Jr., et al., 424/85.2; 514/21; 530/351 [IMAGE AVAILABLE]
17. 5,298,420, Mar. 29, 1994, ****Antibodies**** specific for isotype specific domains of human IgM and human IgG expressed or the B cell

surface; Tse W. Chang, 435/240.27, 69.6, 252.3; 530/387.3, 387.9, 388.73
[IMAGE AVAILABLE]

18. 5,298,407, Mar. 29, 1994, DNA encoding a protein active in lymphocyte-mediated cytotoxicity; Paul J. Anderson, et al., 435/69.1, 6, 240.2, 240.27, 320.1; 530/350, 387.9, 388.73, 388.75; 536/23.5, 24.31
[IMAGE AVAILABLE]

19. 5,298,400, Mar. 29, 1994, Polynucleotide constructs for secreted glycosylated plasminogen activator inhibitor-2 (PAI-2); Peter L. Whitfeld, et al., 435/69.8, 69.2, 172.3, 240.1, 240.2, 320.1 [IMAGE AVAILABLE]

20. 5,292,642, Mar. 8, 1994, ****Methods**** and compositions for the detection of monocyte cytotoxicity inducing factor; C. Michael Jones, 435/7.24, 7.92, 810; 436/64, 548; 530/351, 388.23, 389.2 [IMAGE AVAILABLE]

21. 5,292,636, Mar. 8, 1994, ****Therapeutic**** and diagnostic ****methods**** using soluble T cell surface molecules; Patrick C. Kung, et al., 435/5, 7.23, 7.24, 7.9, 7.94, 34, 974, 975; 436/506, 518, 536, 548, 811, 813
[IMAGE AVAILABLE]

22. 5,286,482, Feb. 15, 1994, ****Methods**** and compositions for inducing monocyte cytotoxicity; C. Michael Jones, 424/85.1, 85.2; 514/2, 8, 21
[IMAGE AVAILABLE]

23. 5,284,935, Feb. 8, 1994, MHC-mediated toxic conjugates useful in ameliorating autoimmunity; Brian R. Clark, et al., 424/185.1, 193.1, 810; 530/395, 403, 806, 807, 868 [IMAGE AVAILABLE]

24. 5,284,931, Feb. 8, 1994, Intercellular adhesion molecules, and their ****binding**** ligands; Timothy A. Springer, et al., 424/139.1, 152.1, 153.1, 154.1, 172.1, 173.1; 514/8; 530/388.22, 395, 808, 868 [IMAGE AVAILABLE]

25. 5,283,058, Feb. 1, 1994, ****Methods**** for inhibiting rejection of transplanted tissue; Denise Faustman, 424/152.1, 172.1, 809, 810 [IMAGE AVAILABLE]

26. 5,274,075, Dec. 28, 1993, Newly identified human epsilon immunoglobulin peptides and related products; Tse W. Chang, 530/324, 387.1, 387.9 [IMAGE AVAILABLE]

27. 5,262,321, Nov. 16, 1993, DNA encoding p107 tumor suppressor; David M. Livingston, et al., 435/240.2, 252.3, 252.33; 536/23.5 [IMAGE AVAILABLE]

28. 5,260,422, Nov. 9, 1993, MHC conjugates useful in ameliorating autoimmunity; Brian R. Clark, et al., 424/185.1, 193.1, 810; 530/402, 403, 868 [IMAGE AVAILABLE]

29. 5,256,561, Oct. 26, 1993, ****Monoclonal**** ****antibody**** to HIV-2 and

uses thereof; Jade Chin, 435/240.27, 5, 974; 530/387.1, 388.1, 388.2, 388.3, 388.35; 935/89, 95, 102, 104 [IMAGE AVAILABLE]

30. 5,252,479, Oct. 12, 1993, Safe vector for gene **therapy**; Arun Srivastava, 435/235.1, 240.2, 320.1 [IMAGE AVAILABLE]

31. 5,244,792, Sep. 14, 1993, Expression of recombinant glycoprotein B from herpes simplex virus; Rae L. Burke, et al., 435/69.3; 424/186.1, 231.1; 435/69.1, 70.3, 71.1, 172.3, 240.2, 254.2, 320.1; 536/23.72; 935/12, 69, 70 [IMAGE AVAILABLE]

32. 5,243,041, Sep. 7, 1993, DNA vector with isolated CDNA gene encoding metalloproteinase; Jose A. Fernandez-Pol, 536/23.5, 24.31 [IMAGE AVAILABLE]

33. 5,242,829, Sep. 7, 1993, Recombinant pseudorabies virus; Dennis L. Panicali, et al., 435/320.1; 424/199.1, 229.1, 232.1; 435/69.1, 69.3, 172.3 [IMAGE AVAILABLE]

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37. 5,229,500, Jul. 20, 1993, Brain derived neurotrophic factor; Yves-Alain Barde, et al., 514/12; 435/69.1; 530/350, 387.9, 389.2, 399, 412, 413 [IMAGE AVAILABLE]

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47. 5,194,593, Mar. 16, 1993, ****Antibodies**** to natural killer cell and non-specific cytotoxic cell receptor and target cell antigens; Donald L. Evans, 530/388.73, 387.1, 389.1 [IMAGE AVAILABLE]
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53. 5,183,734, Feb. 2, 1993, ****Antibodies****, diagnostic systems and ****methods**** for assaying SV40 HBxAg; Ann M. Moriarty, 435/5, 975; 436/512, 820; 530/389.4 [IMAGE AVAILABLE]

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63. 5,128,321, Jul. 7, 1992, PDGF analogs and ****methods**** of use; Mark J. Murray, et al., 514/12, 970; 530/300, 324, 350, 399 [IMAGE AVAILABLE]
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McAnalley, et al., 424/85.2; 514/54, 885 [IMAGE AVAILABLE]

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97. 4,713,324, Dec. 15, 1987, Inverted latency specific ****binding**** assay; John P. Fox, et al., 435/4, 7.21, 7.5, 7.8, 7.9, 7.91, 8, 14, 25, 28, 966, 968; 436/520, 522, 537, 546, 829 [IMAGE AVAILABLE]
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100. 4,676,980, Jun. 30, 1987, Target specific cross-linked heteroantibodies; David M. Segal, et al., 424/136.1, 143.1, 144.1, 152.1, 154.1, 155.1; 435/107, 188; 436/819; 530/388.22, 388.8, 389.1, 389.8, 391.1 [IMAGE AVAILABLE]
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specificity to human small cell carcinoma and use thereof; Samuel D. Bernal, 435/7.23; 424/140.1, 156.1, 178.1, 183.1; 435/70.21, 172.1, 240.27, 259; 436/64, 507, 545, 546, 813, 821; 530/388.85, 391.3, 391.7, 864 [IMAGE AVAILABLE]

103. 4,443,427, Apr. 17, 1984, **Monoclonal** **antibody**; Ellis L. Reinherz, et al., 530/388.75; 424/154.1, 178.1, 183.1; 435/7.24, 70.21, 172.2; 436/548; 530/391.3, 391.7, 864, 868; 600/3; 935/103, 107 [IMAGE AVAILABLE]

E = Anti-C5

0 ANTIC5
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10781 C5
15888 ANTIBOD?

L20 4 (ANTIC5 OR ANTI(W)C5)(L)ANTIBOD?

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L21 3 L20 NOT (L5 OR L17)

=> d 1-3 .bevpat; s bb5(w)1 or bb51

US PAT NO: 4,978,621 [IMAGE AVAILABLE]

L21: 1 of 3

DATE ISSUED: Dec. 18, 1990

INVENTOR: Feroza Ardeshir, San Diego, CA
Janette E. Flint, Del Mar, CA
Robert T. Reese, La Jolla, CA

SEARCH-FLD: 435/68, 172.1, 172.3, 252.33, 320, 243, 69.1, 69.8, 71.2, 91; 935/18, 27, 41, 47, 56, 65, 73; 536/27

ABSTRACT:

DNA sequences are described which encode Plasmodium falciparum merozoite antigenic surface proteins and protein fragments. Corresponding recombinant plasmids and transformed bacterial strains are described. The proteins and fragments have utility for immunological and diagnostic purposes.

US PAT NO: 4,820,635 [IMAGE AVAILABLE]

L21: 2 of 3

DATE ISSUED: Apr. 11, 1989

INVENTOR: Martin E. Sanders, Gaithersburg, MD
Keith A. Joiner, Rockville, MD
Michael M. Frank, Bethesda, MD
Carl H. Hammer, Gaithersburg, MD

SEARCH-FLD: 435/7, 18, 19, 23; 436/821, 540

ABSTRACT:

A kit for assaying the activation of terminal complement cascade is disclosed. The kit includes a plurality of containers which contain a first antibody having a specificity for poly C9 neoantigen. The containers further have a second antibody which is different from the first antibody and has a specificity for a constituent of terminal complement cascade. A third antibody is optionally present which recognizes the second antibody. The kit also includes a substrate splitting enzyme, a substrate for the enzyme which produces a color reaction when split, and a SCb-9 standard microtiter plate. Pipettes and

instructions for performing the assay are also included.

US PAT NO: 4,722,890 [IMAGE AVAILABLE] L21: 3 of 3

DATE ISSUED: Feb. 2, 1988

INVENTOR: Martin E. Sanders, Gaithersburg, MD

Keith A. Joiner, Rockville, MD

Michael M. Frank, Bethesda, MD

Carl H. Hammer, Gaithersburg, MD

SEARCH-FLD: 435/7, 536; 436/821

ABSTRACT:

The present invention discloses an enzyme-linked immunosorbent assay (ELISA) to quantitate fluid phase terminal complement activation. Upon activation to form C5b-9, terminal complement components express neoantigens not present in the unassembled individual components. Rabbit antiserum to polymerized C9 was rendered specific for C9 neoantigenic determinants by serial immunosorbition with human serum, human C9, and other terminal complement components bound to Sepharose. Using the IgG from this antiserum, a sandwich ELISA was devised to bind SC5b-9 from solution onto polystyrene plates. The ELISA plates were developed with the use of goat antiserum to native C9 epitopes followed by a swine anti-goat IgG alkaline phosphatase conjugate. Quantitation of SC5b-9 in solution was performed by comparing sample OD to a standard curve generated with human SC5b-9 that was purified from zymosan-activated serum. The assay is sensitive to as little as 100 ng of SC5b-9/ml and is useful for screening plasma, serum, cerebrospinal fluid, or other biological fluids for the presence of terminal complement cascade activation.

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	12821	C5
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S2	16403	AU=(WANG, Y? OR WANG Y?)
	67	AU=MATIS, L?
	198	AU=MATIS L?
S3	265	AU=(MATIS, L? OR MATIS L?)
	87	AU=ROLLINS S?
	19	AU=ROLLINS, S?
S4	106	AU=(ROLLINS S? OR ROLLINS, S?)

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Still's disease: experience in 12 children.
Wang YJ; Lee YP; Chi CS
Department of Pediatrics, Taichung Veterans General Hospital, Taiwan,
R.O.C.

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Over a 9-year period, twelve patients (8 boys, 4 girls), from 3 to 14 years old, were diagnosed as having Still's disease. Intermittent spiking high fever, poly- or pauci- articular arthritis, and typical evanescent skin rash were the most prominent clinical features. Hemogram examinations showed that 36% of the patients had anemia, ninety-two percent had neutrophilic leukocytosis and 78% had thrombocytosis. Serologically, none had positive results of rheumatoid factor and anti-nuclear antibody. Serum ferritin level was obtained from six patients and all revealed marked elevation during active disease. C-reactive protein and erythrocyte sedimentation rate were both invariably elevated. Immunologically, elevated serum concentrations of IgG, IgA, and *complements* (C3, C4) were found in 33%, 20%, and 17%, respectively. Furthermore, eighty percent of patients showed an increased serum level of circulating *immune* *complexes*. Aspirin (ASA) was used in all patients, but 92% of them required non-steroid antiinflammatory drugs (NSAIDs) in combination to get a better response. Sixty-seven percent of patients needed corticosteroids to control the acute systemic manifestations. Other disease-modifying agents were also used in 33% of our patients. ASA-induced liver function impairment was found in two cases. In addition, one patient experienced an episode of upper gastrointestinal bleeding. Generally speaking, the overall prognosis was good. One patient (8%) died of internal bleeding after a needle liver biopsy.

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11/3,AB/1 (Item 1 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11172291 BIOSIS Number: 97372291

Evidence that activation of human T cells by porcine endothelium involves direct recognition of porcine SLA and costimulation by porcine ligands for LFA-1 and CD2

Rollins S A; Kennedy S P; Chodera A J; Elliott E A; Zavoico G B; *Matis L A*

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Transplantation (Baltimore) 57 (12). 1994. 1709-1716.

Full Journal Title: Transplantation (Baltimore)

ISSN: 0041-1337

Language: ENGLISH

In this study we present a comprehensive evaluation of the molecular interactions between human T cells and porcine aortic endothelial cells (PAEC) that contribute to human T cell activation. Binding assays demonstrated that porcine erythrocytes (E) and PAEC express ligand(s) for the human T cell glycoprotein CD2. Prior incubation of human T cells with a blocking monoclonal antibody directed against CD2 (alpha-CD2-BL) completely inhibited T cell/E and T cell/PAEC interaction. Xenogeneic mixed lymphocyte reactions (XMLR) revealed that human PBMC, or highly purified T cells were activated by PAEC in the absence of human antigen-presenting cells (APC). Addition of alpha-CD2-BL or alpha-LFA-1 to these assays inhibited PAEC-mediated human T cell activation. Furthermore, we demonstrated that highly purified human CD4+ and CD8+ T cells proliferated in response to PAEC and that this response was blocked by monoclonal antibodies directed against LFA-1 and CD2. Addition of alpha-SLA class I blocked the proliferation of CD8+ but not CD4+ T cells, indicating direct presentation of SLA class I antigens to human T cells. We have recently shown that expression of the human *complement* inhibitor (CD59) on PAEC (PAEC-LXSNCD59) rendered these cells resistant to human *complement*-mediated activation and lysis, suggesting that human CD59 expression on PAEC could be an effective *therapy* for hyperacute rejection (HAR). However, recent studies have shown that in addition to its role as a *complement* inhibitor, CD59 binds human T cell CD2 and contributes to T cell activation. We therefore examined whether human CD59 expression on PAEC augmented the human antiporcine T cell response. We demonstrated that human T cells do not display increased binding to or activation by PAEC-LXSNCD59 relative to PAEC controls. Taken together, our data establish that PAEC directly stimulate human T cells in vitro and that interactions between the human accessory molecules CD2, LFA-1 and their PAEC surface ligands contribute to human T cell activation. In addition, the expression of human CD59 on porcine donor organs may confer resistance to human *complement*-mediated HAR without exacerbating the human antiporcine cellular response.

11/3,AB/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11122676 BIOSIS Number: 97322676

Protection of porcine aortic endothelial cells from *complement*-mediated cell lysis and activation by recombinant human CD59

Kennedy S P; *Rollins S A*; Burton W V; Sims P J; Bothwell A L M; Squinto S P; Zavoico G B

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Transplantation (Baltimore) 57 (10). 1994. 1494-1501.

Full Journal Title: Transplantation (Baltimore)

ISSN: 0041-1337

Language: ENGLISH

Discordant xenogeneic organ transplantation is a potential solution to the critical shortage of suitable donor organs. However, clinical application of xenotransplantation with physiologically suitable organs such as those from the pig, is currently limited by the lack of agents to

prevent antibody and *complement*-mediated hyperacute rejection of the transplanted organ. We have used retrovirus-mediated gene transfer to express the terminal *complement* inhibitor protein, human CD59, in neonatal porcine aortic endothelial cells (nPAEC). Human CD59 was constitutively expressed in nPAECs at levels similar to that of native CD59 in human umbilical vein endothelial cells. The protein was tethered to the cell surface by a glycosylphosphatidylinositol anchor, as demonstrated by its removal following *treatment* with phosphatidylinositol-specific phospholipase C. In a model of antibody-dependent *complement* activation, nPAECs expressing human CD59 were protected from membrane pore formation and cell lysis by *complement* derived from either human or baboon sera. Conversely, nPAECs expressing CD59 were not protected from lysis by rabbit or dog *complement*, indicating that recombinant CD59 retained its species-restricted inhibitory activity. Additionally, CD59 expressed on nPAECs inhibited the C5b-9-dependent generation of membrane prothrombinase activity. Collectively, these data establish that stable expression of human CD59 on xenotypic (porcine) endothelial cells renders these cells resistant to both the cytolytic and procoagulant effects of human *complement*. We propose that expression of recombinant human CD59 on porcine donor organs may prevent *complement*-mediated lysis and activation of endothelial cells that leads to hyperacute rejection.

11/3,AB/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11105662 BIOSIS Number: 97305662

Expression of a functional human *complement* inhibitor in transgenic swine as an approach to abrogate xenogeneic organ rejection

Fodor W L; Williams B L; *Rollins S A*; *Matis L A*; Madri J A; Velander W; Squinto S P

Alexion Pharm. Inc., USA

Clinical Research 42 (2). 1994. 273A.

Full Journal Title: Meeting of the American Federation for Clinical Research, Baltimore, Maryland, USA, April 29-May 2, 1994. Clinical Research

ISSN: 0009-9279

Language: ENGLISH

11/3,AB/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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10923247 BIOSIS Number: 97123247

Inhibition of *complement*-mediated cytolysis by the terminal *complement* inhibitor of herpesvirus saimiri

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Journal of Virology 68 (2). 1994. 730-737.

Full Journal Title: Journal of Virology

ISSN: 0022-538X

Language: ENGLISH

Herpesvirus saimiri (HVS) is a lymphotropic herpesvirus that induces T-cell transformation in vitro and causes lymphomas and leukemias in New World primates other than its natural host, the squirrel monkey. Nucleotide sequence analysis of the HVS genome revealed two open reading frames with significant homology to genes for human *complement* regulatory molecules. One of these genes encodes a predicted protein (designated HVSCD59) with 48% amino acid sequence identity to the human terminal *complement* regulatory protein CD59 (HuCD59). The CD59 homolog from squirrel monkey (SMCD59) was cloned, and the corresponding amino acid sequence showed 69% identity with HVSCD59. BALB/3T3 cells stably expressing HVSCD59, SMCD59, or

HuCD59 were equally protected from *complement*-mediated lysis by human serum. However, only HVSCD59-expressing cells were effectively protected from *complement*-mediated lysis when challenged with rat serum, suggesting that HVSCD59 was less species restrictive. The *complement* regulatory activity of HVSCD59 and SMCD59 occurred after C3b deposition, indicating terminal *complement* inhibition. *Treatment* of BALB/3T3 stable transfectants with phosphatidylinositol-specific phospholipase C prior to *complement* attack decreased the *complement* regulatory function of HVSCD59, suggesting cell surface attachment via a glycosyl-phosphatidylinositol anchor. Cells expressing HVSCD59 effectively inhibited *complement* -mediated lysis by squirrel monkey serum in comparison with SMCD59-expressing cells. Finally HVSCD59-specific transcripts were detected in owl monkey cells permissive for lytic HVS replication but not in T cells transformed by HVS, which failed to produce virions. These data are the first to demonstrate a functional, virally encoded terminal *complement* inhibitor and suggest that HVSCD59 represents a humoral immune evasion mechanism supporting the lytic life cycle of HVS.

11/3,AB/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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7648068 BIOSIS Number: 90016068

THE *COMPLEMENT*-INHIBITORY ACTIVITY OF CD59 RESIDES IN ITS CAPACITY TO BLOCK INCORPORATION OF C9 INTO MEMBRANE C5B-9

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J IMMUNOL 144 (9). 1990. 3478-3483. CODEN: JOIMA

Full Journal Title: Journal of Immunology

Language: ENGLISH

A human E membrane protein that inhibits lysis by the purified human C5b-9 proteins was isolated and characterized. After final purification, the protein migrated as an 18- to 20-kDa band by SDS-PAGE. Elution from gels slices and functional assay after SDS-PAGE (nonreduced) confirmed that all C5b-9 inhibitory activity of the purified protein resided in the 18- to 20-kDa band. Phosphatidylinositol-specific phospholipase C digestion of the purified protein abolished 50% of its C5b-9 inhibitory activity, and removed approximately 15% of the protein from human E. Western blots of normal and paroxysmal nocturnal hemoglobinuria E revealed an absence of the 18- to 20-kDa protein in the paroxysmal nocturnal hemoglobinuria E cells. The identity of this E protein with leukocyte Ag CD59 (Pl8, HRF20) was confirmed immunochemically and by N-terminal amino acid sequence analysis. A blocking antibody raised against the purified protein reacted with a single 18- to 20-kDa band on Western blots of human erythrocyte membranes. Prior incubation of human E with the F(ab) of this antibody increased subsequent lysis by the purified human C5b-9 proteins. Potentiation of C5b-9-mediated lysis was observed when erythrocytes were preincubated with this blocking antibody before C5b-9 assembly was initiated, or, when this antibody was added after 30 min, 0.degree. C incubation of C5b-8-*treated* E with C9. Chicken E incubated with purified CD59 were used to further characterize the mechanism of its C-inhibitory activity. Preincorporation of CD59 into these cells inhibited lysis by C5b-9, regardless of whether CD59 was added before or after assembly of the C5b-8 complex. When incorporated into the membrane, CD59 inhibited binding of 125I-C9 to membrane C5b-8 and reduced the extent of formation of SDS-resistant C9 polymer. The inhibitory effect of CD59 on 125I-C9 incorporation was most pronounced at near-saturating input of C9 (to C5b-8). By contrast, CD59 did not inhibit either C5b67 deposition onto the cell surface, or, binding of 125I-C8 to preassembled membrane C5b67. Taken together, these data suggest that CD59 exerts its C-inhibitory activity by limiting incorporation of multiple C9 into the membrane C5b-9 complex.

11/3,AB/6 (Item 6 from file: 55)

7374902 BIOSIS Number: 89025921

REGULATORY CONTROL OF *COMPLEMENT* ON BLOOD PLATELETS MODULATION OF
PLATELET PROCOAGULANT RESPONSES BY A MEMBRANE INHIBITOR OF THE C5B-9
COMPLEX

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J BIOL CHEM 264 (32). 1989. 19228-19235. CODEN: JBCHA

Full Journal Title: Journal of Biological Chemistry

Language: ENGLISH

Antibody against a membrane inhibitor of the C5b-9 complex has been used to investigate regulatory control of the terminal *complement* proteins on blood platelets. Monospecific rabbit antibody (.alpha.-Pl8) was raised against the purified 18-kDa erythrocyte membrane inhibitor of C5b-9 (Sugita, Y., Nakano, Y., and Tomita, M. (1988) J. Biochem. (Tokyo) 104, 633-637). In addition to its interaction with erythrocytes, this antibody (and its Fab) bound specifically to platelet membranes. In immunoblots of cell membrane proteins prepared under non-reducing conditions, .alpha.-Pl8 bound specifically to an 18-kDa erythrocyte membrane protein and to a 37-kDa platelet membrane protein. Absorption of this antibody by platelet membranes competed its binding to the purified 18-kDa erythrocyte protein, suggesting that epitopes expressed by the erythrocyte 18-kDa C5b-9 inhibitor are common to the platelet. When bound to the platelet surface, the Fab of .alpha.-Pl8 increased C9 activation by membrane C5b-8, monitored by exposure of a complex-dependent C9 neoepitope. Although .alpha.-Pl8 caused little increase in the cytolysis of platelets *treated* with C5b-9 (total release of lactate dehydrogenase < 5%), it markedly increased the cell stimulatory responses induced by these *complement* proteins, including, secretion from platelet .alpha.- and dense granules, conformational activation of cell surface GP IIb-IIIa, release of membrane microparticles from the platelet surface, and exposure of new membrane binding sites for components of the prothrombinase enzyme complex. Prior incubation of C5b67 platelets with 100 .mu.g/ml .alpha.-Pl8 (Fab) lowered by approximately 10-fold the half-maximal concentration of C8 required to elicit each of these responses (in the presence of excess C9). Incubation with .alpha.-Pl8 (Fab) alone did not activate platelets, nor did incubation with this antibody potentiate the stimulatory responses of platelets exposed to other agonists. These data indicate that a membrane inhibitor of the C5b-9 complex normally serves to attenuate the procoagulant responses of blood platelets exposed to activated *complement* proteins, and suggest the mechanism by which a deletion or inactivation of this cell surface component would increase the risk of vascular thrombosis.

11/3,AB/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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7209767 BIOSIS Number: 88132512

TUMOR CELLS *TREATED* WITH VACCINIA VIRUS CAN ACTIVATE THE ALTERNATIVE
PATHWAY OF MOUSE *COMPLEMENT*

WAKAMIYA N; OKADA N; *WANG Y-L*; ITO T; UEDA S; KATO S; OKADA H

DEP. PATHOL., RES. INST. MICROBIAL DIS., OSAKA UNIV., 3-1 YAMADAOKA,
SUITA, OSAKA 565.

JPN J CANCER RES 80 (8). 1989. 765-770. CODEN: JJCRE

Full Journal Title: Japanese Journal of Cancer Research

Language: ENGLISH

Vaccinia virus has been shown to render mouse tumor cells highly immunogenic. Since we have demonstrated that induction of *complement* activating capacity on guinea pig tumor cells by Sendai virus infection causes the tumor cells to become immunogenic, we assumed that vaccinia virus infection of mouse tumor cells might render them reactive with homologous mouse *complement*. Therefore, murine tumor cells, MH134 and

X5563, infected with vaccinia virus (VV) were incubated with mouse plasma and C3 deposition was determined by staining with fluorescein isothiocyanate-labeled anti-C3. We found that VV-infected tumor cells possess the ability to activate the alternative *complement* pathway (ACP) of murine *complement*. For induction of *complement* activating ability, at least a 3 h incubation of the infected MHL34 cells was required indicating that the generation of ACP-activating capacity on MHL34 infected with VV is time-dependent. Furthermore, ultraviolet-irradiated vaccinia virus was able to induce ACP-activating capacity on tumor cells as well.

11/3,AB/8 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE
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7391489 EMBASE No: 89108109
Multi-stage, multi-force dewatering of steelmaking sludges
Watson J.L.; *Wang Y.*
Department of Metallurgical Engineering, University of Missouri-Rolla,
Rolla, MO 65401 USA
POWDER TECHNOL. (Netherlands) , 1989, 58/1 (49-53) CODEN: POTE B ISSN:
0032-5910

LANGUAGES: English
A novel, sequential, multi-stage, multi-force dewatering process for steelmaking sludges is described. The process consist of stages of chemical flocculant addition, sedimentation *complemented* by magnetic forces, decantation of clear liquid, and finally filtration to produce a cake. The synergistic effect of the chemical, magnetic and gravity forces results in rapid and complete solid/liquid separation. The results show that blast furnace, basic oxygen furnace, and electric arc furnace sludges can be dewatered to produce cakes containing 70-80 wt.% solids, while discarding clear water, which represents 75-90% of the original sludge volume. Thus this dewatering process has considerable potential for the *treatment* of steelmaking sludged to permit more efficient disposal, storage, or recycle.

11/3,AB/9 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
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08334673 93044673
Electroejaculation in spinal cord injured males.
Wang YH; Chiang HS; Wu CH; Lien IN
Department of Physical Medicine and Rehabilitation, National Taiwan University Hospital, Taipei, R.O.C.
J Formos Med Assoc (HONG KONG) Apr 1992, 91 (4) p413-8, ISSN
0371-7682 Journal Code: BLQ
Languages: ENGLISH
Document type: JOURNAL ARTICLE

Electroejaculation is a newly developed method to retrieve sperm in anejaculatory spinal cord injured (SCI) males. We studied 25 completely traumatic SCI males from August 1990 to May 1991. The patients' ages ranged from 18.7 to 43.3 years, and the interval since injury ranged from four months to 14.1 years. The level of injury varied from *C5* to T12. Bi-directional emission was found in 12 patients, antegrade in nine, retrograde in one and failure in three. Electroejaculatory stimulation parameters were 434 +/- 54 mA for mean maximum current, 21.7 +/- 2.7 volts for mean maximum voltage and 35.9 +/- 3.1 degrees C for mean maximum probe temperature. The antegrade semen obtained showed wide variations in sperm quality and quantity between subjects. The total sperm count was 478 +/- 809 x 10(6) in the antegrade portion, and the sperm motility was below 5% in most cases. The retrograde portion was usually worse. There was no correlation between sperm quality and quantity with patient age, injury level or injury period. Bladder management had no effect on the results of electrical stimulation. Epididymitis had a negative impact on the success of retrieval. Low-level injury victims needed analgesia or anesthesia to

complete the stimulation. The major side effects were minimal autonomic dysreflexia and mild rectal mucosal change. Repeated stimulation may improve sperm counts, but semen quality deteriorates if the procedure is performed once a week. As a whole, electroejaculation is a safe, effective and simple procedure to retrieve sperm in anejaculatory persons, especially SCI patients.

11/3,AB/10 (Item 1 from file: 399)
DIALOG(R)File 399:CA Search(R)
(c) 1994 American Chemical Society. All rts. reserv.

118198171 CA: 118(20)198171c PATENT
Genetically engineered cells as universal donor cells for vascular grafts or drug delivery
INVENTOR(AUTHOR): Sims, Peter J.; Bothwell, Alfred L. M.; Elliot, Eileen A.; Flavell, Richard A.; Madri, Joseph; Rollins, Scott; Bell, Leonard; Squinto, Stephen
LOCATION: USA
ASSIGNEE: Oklahoma Medical Research Foundation; Yale University
PATENT: PCT International ; WO 9302188 A1 DATE: 930204
APPLICATION: WO 92US5920 (920714) *US 729926 (910715) *US 906394 (920629)
PAGES: 88 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/00A; C12N-015/12B; A01K-067/027B; C12N-005/16B; C12N-005/22B; C12N-015/87B; A61L-027/00B; C07K-015/00B DESIGNATED COUNTRIES: CA; JP
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; MC; NL; SE

11/3,AB/11 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI
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009746348 WPI Acc No: 94-026199/03
Related WPI Accession(s): 93-058786
XRAM Acc No: C94-012135
Culture of micro-vascular endothelial cells in patient - by implanting within matrix, of e.g. polymers and attachment molecules for capillary growth e.g. after angioplasty
Patent Assignee: (ALEX-) ALEXION PHARM INC; (OKLA-) OKLAHOMA MED RES FOUND; (UYYA) UNIV YALE
Author (Inventor): BELL L; BOTHWELL A L M; ELLIOT E A; FLAVELL R A; KENNEDY S; MADRI J; *ROLLINS S*; SQUINTO S
Patent Family:
CC Number Kind Date Week
WO 9400560 A1 940106 9403 (Basic)
Priority Data (CC No Date): US 906394 (920629)
Applications (CC,No,Date): WO 93US6216 (930629)
Abstract (Basic): WO 9400560 A

Isolated microvascular endothelial cells (MEC) are cultured in a patient by implanting them into a human or animal within a 3-dimensional matrix which allows the cells to form a 3-dimensional capillary network and also permits vascular anastomosis between this network and the patient's circulation.

The matrix itself is new.

The matrix, whcih is seeded before implantation, is made of natural or synthetic polymer and attachment molecules, partic. laminin, fibronectin, thrombospondin, entactin, proteoglycans, glycosaminoglycans, collagens types 1-12, synthetic molecules contg. peptide binding sites (RGD,LIGRKKT or YIGSR) or their polymers.

Pref. the cells are engineered so that they do not produce class I and/or class II MHC antigens on their surface and may also contain a sequence encoding a *therapeutic* agent.

USE/ADVANTAGE - These MEC are universal donor cells used e.g. for reconstruction of vascular linings (partic. following balloon angioplasty for coronary arterial disease) and for delivery of

therapeutic agents. They can be protected against acute rejection (*complement*-induced lysis); are not subject to attack by T cells and may include a suicide mechanism. Dwg.0/10

11/3,AB/12 (Item 2 from file: 351)
DIALOG(R)File 351:DERWENT WPI
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009365307 WPI Acc No: 93-058786/07
Related WPI Accession(s): 94-026199
XRAM Acc No: C93-026300
XRPX Acc No: N93-044769

Genetically engineered mammalian cell for *treatment* of coronary artery disease - inhibits *complement*-mediated attack and does not express surface proteins encoded by class I or II major histocompatibility complex genes

Patent Assignee: (ALEX-) ALEXION PHARM INC; (OKLA-) OKLAHOMA MED RES FOUND; (UYYA) UNIV YALE

Author (Inventor): BELL L; BOTHWELL A L M; ELLIOT E A; FLAVELL R A; KENNEDY S; MADRI J; *ROLLINS S*; SIMS P J; SQUINTO S

Patent Family:

CC Number	Kind	Date	Week
WO 9302188	A1	930204	9307 (Basic)
EP 591462	A1	940413	9415
AU 9346579	A	940124	9420

Priority Data (CC No Date): US 906394 (920629); US 729926 (910715)

Applications (CC,No,Date): AU 9346579 (930629); WO 92US5920 (920714); EP 92915715 (920714); WO 92US5920 (920714)

Abstract (Basic): WO 9302188 A

Genetically engineered mammalian cells for transplantation into human or animal do not express on their surface proteins encoded by class II (II cells) or class I (I cells) major histocompatibility complex genes which elicit a T lymphocyte mediated reaction against the cell.

Also claimed are: (1) a transgenic or nonhuman animal or an organ from it contg. I or II cells; (2) a prosthesis for implantation in an animal having cells attached that are resistant to *complement* mediated attack or fail to elicit a T lymphocyte mediated attack of the engineered cell when introduced into another animal species; and (3) I or II cells further comprising a nucleotide sequence encoding a *therapeutic* agent.

USE/ADVANTAGE - I and II cells can be used to decrease T cell mediated reaction against transplanted cells, so preventing hyperacute rejection. The cells are resistant to both *complement* and cellular attack when transplanted into a foreign host as they are not recognised as foreign. The cells, e.g. genetically engineered endothelial cells, can be used to reendothelialise a denuded blood vessel, and to deliver *therapeutic* agents to humans or animals. A vector comprising the CD59 *complement* gene may be expressed in cells causing expression of the gene on the cell surface which prevents platelet and endothelial cell activation and cytolysis. The cells can be used to *treat* patients with immune disorders and diseases such as immunovascularities, rheumatoid arthritis, scleroderma, disseminated intravascular coagulation, paroxysmal nocturnal haemoglobinuria, thrombotic thrombolytic purpurs, vascular occlusion, reocclusion after surgery, coronary thrombosis and myocardial infarction.

Dwg.4/9

Processing

3	ANTIC5
504852	ANTI
12821	C5
98	ANTI(W)C5
738426	ANTIBOD?
S12	71 (ANTIC5 OR ANTI(W)C5) AND ANTIBOD?

?s sl2 not (s7 or sl0); rd

E = Anti-C5

71 S12
1 S7
24 S10
S13 71 S12 NOT (S7 OR S10)
>>>Duplicate detection is not supported for File 351.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records (50)
...completed examining records

S14 33 RD (unique items)
?s sl4/ti,de,maj
>>>Term "MAJ" is not defined in one or more files
S15 4 S14/TI,DE,MAJ
?t 15/an,ti/1-4; t 14/3,ab/1-33; s bb5(w)1 or bb51

15/AN,TI/1 (Item 1 from file: 72)
DIALOG(R)File 72:(c) 1994 Elsevier Science B.V. All rts. reserv.

7411214 EMBASE No: 89133448

Binding of complement component C5 to model immune complexes and the use of anti-C5 antibodies for determination of C5-containing circulating immune complexes

15/AN,TI/2 (Item 2 from file: 72)
DIALOG(R)File 72:(c) 1994 Elsevier Science B.V. All rts. reserv.

7408361 EMBASE No: 89130594

Binding of complement components C1Q, C3, C4 and C5 to a model immune complex in ELISA

15/AN,TI/3 (Item 3 from file: 72)
DIALOG(R)File 72:(c) 1994 Elsevier Science B.V. All rts. reserv.

5833451 EMBASE No: 85078961

Bactericidal but not nonbactericidal C5b-9 is associated with distinctive outer membrane proteins in Neisseria gonorrhoeae

15/AN,TI/4 (Item 1 from file: 154)
DIALOG(R)File 154:(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

06643271 88288271

Generation of a monoclonal antibody to mouse C5 application in an ELISA assay for detection of anti-C5 antibodies.

>>>No matching display code(s) found in file(s): 399

14/3,AB/1 (Item 1 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11082550 BIOSIS Number: 97282550

Antibodies against the C2 COOH-terminal region discriminate the active and latent forms of the multicatalytic proteinase complex

Arribas J; Arizti P; Castano J G

Dep. Bioquimica, Inst. Investigaciones Biomedicas del CSIC, Fac. de Medicina de la UAM, 28029 Madrid, SPA

Journal of Biological Chemistry 269 (17). 1994. 12858-12864.

Full Journal Title: Journal of Biological Chemistry

ISSN: 0021-9258

Language: ENGLISH

The mouse cDNA homologues of the rat C2, C9, and C5 subunits of the multicatalytic proteinase have been cloned and expressed in bacteria. The respective recombinant proteins were purified and used to produce specific anti-subunit *antibodies*. Immunoblotting of two-dimensional gels of

purified rat liver multicatalytic proteinase showed that the C2 (32-kDa) and C9 (29-kDa) polypeptides are resolved into three and two isoelectric variants, respectively, likely due to post-translational modifications, i.e. phosphorylation, and the presence of two *anti*-C5* reacting polypeptides (25.5 and 23 kDa). Epitope mapping of the anti-C2-specific *antibody* with different constructs of the recombinant C2 protein allowed us to determine that one major epitope of this anti-C2 *antibody* is located within the last 9-11 amino acids of the C2 polypeptide. Affinity purified *antibodies* directed against the C2 COOH-terminal were able to discriminate the active and latent forms of the multicatalytic proteinase, supporting the conclusion that the C2 protein found in the active form of the enzyme is a polypeptide of 28 kDa, produced by the loss, at least, of the last 9-13 amino acids (DEPAEKADEPMEH) of the intact C2 (32-kDa) component. By in vitro treatment of the latent form of the enzyme with elastase, we show the conversion of the C2 (32-kDa) component to a 28-kDa protein with loss of recognition by the anti-C2 COOH-terminal affinity purified *antibodies*, but this limited degradation of the C2 component did not have any significant effect on the proteolytic activity (assayed with myelin basic protein and fluorogenic peptides) of the multicatalytic proteinase. It is suggested that the proteolytic cleavage of the C2 COOH-terminal region may be involved in the regulation of the interaction of the multicatalytic proteinase with other cellular proteins and/or in the translocation of the complex to the nucleus.

14/3,AB/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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10097374 BIOSIS Number: 95097374

COMPLEMENT ACTIVATION IN SEPTIC BABOONS DETECTED BY NEOEPITOPE-SPECIFIC ASSAYS FOR C3B-IC3B-C3C C5A AND THE TERMINAL C5B-9 COMPLEMENT COMPLEX TCC
MOLLNES T E; REDL H; HOGASEN K; BENGTTSSON A; GARRED P; SPEILBERG L; LEA T
; OPPERMAN M; GOTZE O; SCHLAG G
DEP. IMMUNOL. TRANSFUSION MED., N-8017 NORDLAND CENTRAL HOSP., BODO,
NORWAY.

CLIN EXP IMMUNOL 91 (2). 1993. 295-300. CODEN: CEXIA
Full Journal Title: Clinical and Experimental Immunology
Language: ENGLISH

We have investigated the cross-reactivity of various species in neoepitope-specific methods for quantification of human complement activation products. In contrast to most other species examined, baboon showed a substantial cross-reactivity supporting a high degree of homology between human and baboon complement. An assay for C3b, iC3b and C3c (MoAb bH6) showed moderately good reactivity, in contrast to a C3a assay which did not cross-react. Excellent reactivity was found for C5a using MoAbs C17/5 and G25/2. The reactivity of an established TCC assay (MoAb aE11 to a C9 neoepitope and polyclonal *antibody* to C5) was improved substantially by replacing the *anti*-C5* *antibody* with a new MoAb to C6 particularly selected on the basis of baboon cross-reactivity. Plasma samples from baboons receiving 2.5 .times. 10⁹ and 1.0 .times. 10¹⁰ live Escherichia coli bacteria/kg were examined with the assays described. In vivo complement activation with the lowest dose was moderate and kept under control, in contrast to the highest dose, where an uncontrolled increase in all activation products continued throughout the infusion period. These results support the hypothesis that sufficiently high amounts of endotoxin lead to uncontrolled activation of complement as seen in irreversible septic shock. The results are discussed with particular emphasis on activation of the terminal complement pathway.

14/3,AB/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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9100540 BIOSIS Number: 93085540

BACTERICIDAL ACTIVITY OF C9-DEFICIENT HUMAN SERUM
PRAMOONJAGO P; KINOSHITA T; HONG K; TAKATA-KOZONO Y; KOZONO H; INAGI R;
INOUE K

DEP. BACTERIOL., OSAKA UNIV. MED. SCH., SUITA, OSAKA 565, JAPAN.

J IMMUNOL 148 (3). 1992. 837-843. CODEN: JOIMA

Full Journal Title: Journal of Immunology

Language: ENGLISH

Escherichia coli B/SM, strain 1-1, was killed dose dependently by human hereditary C9-deficient serum (C9DHS), which was shown to contain no C9 Ag by an ELISA method. On the other hand, human hereditary C7-deficient serum did not kill the bacteria under similar conditions. The bactericidal activity of C9DHS was inhibited by rabbit *anti*-C5 *antibody* but not by murine anti-C9 mAb. The anti-C9 *antibody* decreased the bactericidal activity of normal human serum (NHS) to the level of that with C9DHS. Sheep anti-human lysozyme *antibody* did not affect the bactericidal activity of C9DHS or NHS even when added at more than twice the concentration required to block the serum lysozyme activity on Micrococcus luteus. After treatment with C9DHS and washing, surviving Escherichia coli were killed by C9, but not by lysozyme, transferrin, or both. Other strains of E. coli (K12 W3110, C600, and NIHJ) and Salmonella typhimurium (strain NCTC 74), all maintained in the laboratory, were also killed by C9DHS. However, pathogenic strains recently isolated from patients with traveler's diarrhea and some strains of S. typhimurium were resistant to both C9DHS and NHS, at least at the serum concentration tested. A concentration of 0.1 M Tris did not increase the susceptibility of serum-resistant strains of bacteria to C9DHS, but made one strain of S. typhimurium tested susceptible to NHS, but not to C9DHS. These results clearly showed that C9DHS kills bacteria that are sensitive to NHS through activation of C up to the step of C8 in the same way that C9-deficient C serum lysed sensitized erythrocytes.

14/3,AB/4 (Item 4 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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9043942 BIOSIS Number: 93028942

INDUCTION OF ACTIVE IMMUNOLOGICAL HYPO-NON-RESPONSIVENESS TO C5 IN ADULT
C5-DEFICIENT DBA-2 MICE

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IMMUNOLOGY 74 (3). 1991. 380-385. CODEN: IMMUA

Full Journal Title: Immunology

Language: ENGLISH

Injection of C5-sufficient BALB/c serum rendered DBA/2 mice (C5-deficient) immunologically hypo- or non-responsive to C5. This was indicated by C5-elimination studies in the C5-deficient mice showing similar half-lives for C5 upon single and repeated BALB/c serum injection. Concrete evidence for C5 non-responsiveness came from experiments showing that C5-injected DBA/2 mice were unable to mount an *anti*-C5 *antibody* response after active immunization with C5-sufficient serum in Freund's complete adjuvant. C5 hypo/non-responsiveness could be induced in DBA/2 mice via the intravenous as well as the intraperitoneal route, provided the C5-sufficient serum was administered in the very narrow dose range of 10-100 μ l (apprx. 0.3-3 μ g of C5). Upon i.v. C5 injection, C5 non-responsiveness was nearly complete on Day 4 and lasted about 3 weeks. Hyporesponsiveness was still present 6 weeks after serum injection. C3-/C5-depleting cobra venom factor reversed tolerization for C5, at least when applied within 48 hr after i.v. C5 injection. Similarity between the acquired C5 hypo/non-responsiveness of DBA/2 mice and the established C5 tolerance of BALB/c mice was suggested by adoptive cell transfer experiments: spleen cells from naive DBA/2 mice stimulated B cells of C5-sufficient nude mice to produce C5-neutralizing *antibodies*. In contrast, splenocytes from C5-tolerized DBA/2 mice, like those of BALB/c mice, did not decrease haemolytic C5 levels in C5-sufficient nude mice.

14/3,AB/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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8611431 BIOSIS Number: 92076431

C3 AND T-CELL-DEPENDENT ADJUVANT ACTIVITY OF IN-VIVO FORMED IMMUNE COMPLEXES

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IMMUNOLOGY 73 (3). 1991. 264-270. CODEN: IMMUA

Full Journal Title: Immunology

Language: ENGLISH

The effects of polyclonal *antibodies* to mouse serum components on the primary humoral immune response of mice in vivo were studied. It was observed that rabbit IgG to complement component C3 and albumin and mouse IgG to C5, but also heat-aggregated non-immune rabbit IgG, enhanced the agglutinating *antibody* response to sheep erythrocytes (SRBC). Since the increase in response was only observed when antigen and *antibodies* were administered via the same route (i.p.), immunological adjuvant activity was implicated. Ineffectiveness of *anti*-C5 IgG in C5-deficient mice indicated that the *antibody*-induced adjuvant activity is mediated by in vivo formed immune complexes (IC). The adjuvant activity of IC was reduced by selective C3-depletion of animals, pointing to a requirement of C3. The effect of variations in other parameters was studied with anti-C3 and *anti*-C5 IgG as immunoadjuvant. The immunostimulatory effect was most pronounced when the *antibodies* were administered simultaneously with or shortly before antigen. Treatment of animals with *antibodies* one or two days before antigen, however, resulted in a suppression of the response. The response to thymus-independent antigens was not enhanced by anti-C3 nor by *anti*-C5 IgG. Optimal adjuvant activity of anti-C3 IgG was observed at low antigen doses. Nude mice were insensitive to the immunopotentiating effect of anti-C3 and so was the F1 progeny of BALB/c .male. and CBA/N.female. mice expressing a B-cell maturation defect. C5 deficiency and lipopolysaccharide (LPS) non-responsiveness did not affect the adjuvant activity of in vivo formed C3-anti-C3 IC.

14/3,AB/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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7648021 BIOSIS Number: 90016021

MODULATION OF ALVEOLAR MACROPHAGE LEUKOTRIENE B4 RELEASED BY COMPLEMENT COMPONENT C5

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J LAB CLIN MED 115 (4). 1990. 497-503. CODEN: JLCMA

Full Journal Title: Journal of Laboratory and Clinical Medicine

Language: ENGLISH

The release of neutrophil chemotactic activity by the guinea pig alveolar macrophage (AM) is dependent on the fifth component of complement (C5) on the cell surface. Because one potent chemotactic factor released by AMs is leukotriene B4 (LTB4), we hypothesized that cell surface C5 may modulate LTB4 release. To test this hypothesis, human AMs obtained by bronchoalveolar lavage from 12 subjects were cultured for 4 hours in the presence of *anti*-C5 Fab' *antibodies* with stimuli. The cultures were harvested and evaluated for LTB4 by radioimmunoassay. The LTB4 levels in supernatants obtained from AMs cultured in media alone were variable (447 .+- . 63 pg/ml), but the levels were increased when AMs were cultured with the stimuli-opsonized zymosan, immune complexes, or lipopolysaccharide (233%, 49%, and 114% increase, respectively, compared with macrophages

cultured in media alone, $p < 0.05$). Culturing the AMs with *anti*-C5* Fab' *antibodies* inhibited the release of LTB4 induced by opsonized zymosan, immune complexes, or lipopolysaccharide (78%, 41%, and 82% inhibition, respectively, $p < 0.05$). Consistent with these observations, *anti*-C5* Fab' *antibodies* also decreased the neutrophil chemotactic activity of culture supernatant obtained from AMs stimulated with the same stimuli ($p < 0.001$). These data suggest that AM release of LTB4 may be C5-dependent.

14/3,AB/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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7432232 BIOSIS Number: 89083251

SYNTHESIS OF COMPLEMENT BY ALVEOLAR MACROPHAGES FROM PATIENTS WITH SARCOIDOSIS

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SCAND J IMMUNOL 31 (1). 1990. 15-24. CODEN: SJIMA

Full Journal Title: Scandinavian Journal of Immunology

Language: ENGLISH

Sarcoidosis is a granulomatous disorder of unknown aetiology. Alveolar macrophages (AM) in sarcoidosis release a variety of mediators important to the pathogenesis of the disease. Complement is essential for the inflammatory response and we investigated whether there were any major defects in the potential for sarcoidosis AM to synthesize complement in vitro. AM from 11 patients with active sarcoidosis and three healthy controls were cultured under serum-free conditions. There was a significant binding of polyclonal (*anti*-C5*, -C6, -C7, -C8) and monoclonal anti-complement *antibodies* (anti-C3c and anti-C9 neoepitope (aE11)) to agarose beads incubated with unstimulated AM for 24, 48, or 72 h. A significant and inhibitable production of soluble C3c, C5, C9, and S-protein was found in the harvested medium as detected by enzyme immunoassays. Activated C3 and C9 were also detected based on neoepitope expression. Presence of co-cultured agarose beads reduced the amount of soluble S-protein due to deposition on the agarose. We argue that the C9 neoepitope is an integral part of the terminal complement complex (TCC), both in the fluid and solid phase when bound to the agarose. In the fluid phase, SC5b-9 was generated, whereas the agarose-bound S-protein is assumed not to be associated with TCC on the beads. The results demonstrate for the first time that AM from sarcoidosis patients synthesize the functional alternative and terminal pathway of complement.

14/3,AB/8 (Item 8 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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7385697 BIOSIS Number: 89036716

AN IMMUNOLOGICAL DETERMINANT OF RNASE P PROTEIN IS CONSERVED BETWEEN ESCHERICHIA-COLI AND HUMANS

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DEP. BIOL., YALE UNIV., NEW HAVEN, CONN. 06520.

PROC NATL ACAD SCI U S A 86 (22). 1989. 8717-8721. CODEN: PNASA

Full Journal Title: Proceedings of the National Academy of Sciences of the United States of America

Language: ENGLISH

RNase P, an enzyme with RNA and protein subunits, cleaves tRNA precursor molecules to form the 5' termini of mature tRNAs in both prokaryotes and eukaryotes. Rabbit *antibodies* made against the protein subunit, C5 protein, of Escherichia coli RNase P bound RNase P protein from E. coli and Bacillus subtilis in immunoblots and solid-phase immunoassays. These rabbit *anti*-C5* *antibodies* also bound a protein (Mr .apprxeq. 40,000) in preparations of RNase P from human (HeLa) cells and depleted the enzymatic activity from preparations of RNase P from both human and E. coli cells. Finally, rabbit *anti*-C5* *antibodies* immunoprecipitated from crude

extracts of human cells a ribonucleoprotein complex containing H1 RNA, the putative RNA component of human RNase P. These results show that an antigenic determinant is shared by C5 protein from E. coli RNase P and a protein component of RNase P from human cells.

14/3,AB/9 (Item 9 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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7092945 BIOSIS Number: 88015690

BINDING OF COMPLEMENT COMPONENTS C1q C3 C4 AND C5 TO A MODEL IMMUNE COMPLEX IN ELISA

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J IMMUNOL METHODS 119 (1). 1989. 103-110. CODEN: JIMMB

Full Journal Title: Journal of Immunological Methods

Language: ENGLISH

When normal human serum is added to microELISA plates coated with monomeric or aggregated IgG various complement components become bound and can be detected with specific chicken anti-C1q, anti-C3, anti-C4 and *anti*-C5* antibodies*. Using such assays we found increased C1q- and decreased C3- and C4-binding in sera from patients with SLE. In contrast, sera from patients with rheumatoid arthritis showed decreased C3 binding but normal C1q binding. The decreases in C3 and C4 binding observed in the sera from patients with SLE were larger than the corresponding decreases determined by radial immunodiffusion. Comparing these results with those of the CH50 assay, the correlation coefficient between CH50 and the C3-binding assay was 0.48. There was no correlation between the results of the CH50 and those of the C1q-, C4- or C5-binding assays.

14/3,AB/10 (Item 10 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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6571412 BIOSIS Number: 86037963

A SENSITIVE METHOD TO DETECT SYNTHESIS OF THE FUNCTIONAL CLASSICAL ALTERNATIVE AND TERMINAL PATHWAY OF COMPLEMENT BY CELLS CULTURED IN-VITRO

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SCAND J CLIN LAB INVEST 48 (3). 1988. 223-232. CODEN: SJCLA

Full Journal Title: Scandinavian Journal of Clinical and Laboratory Investigation

Language: ENGLISH

A new method used to study in vitro synthesis by human monocytes and alveolar macrophages of the essential complement components for the functional classical, alternative and terminal pathway is presented. The method is based on accumulation of major complement components on activators of the alternative (agarose beads) and classical (IGM-sensitized sheep erythrocytes; ElgM) pathway during co-culture with the phagocytes. There was a time-dependent increase in binding of labelled protein to the co-cultured activator, demonstrating de novo protein synthesis by the phagocytes. Moreover, there was a significant binding to the co-cultured agarose beads and ElgM of monoclonal anti-C3c, anti-C3g, polyclonal *anti*-C5*-C9 and of two monoclonal *antibodies* (poly C9-MA and MCAEl1) to a neoantigen of polymerized C9 present in the terminal complement complex (TCC). In addition, we found a significant binding of polyclonal anti-C4 *antibodies* to co-cultured ElgM. Incubation of the activators in human serum, subsequently revealed the same pattern of *antibody* binding. There was no binding of anti-S protein *antibodies* to the activators after incubation with serum or with the phagocytes. We thus conclude that mononuclear phagocyte-produced complement in the form of C3b, iC3b, and the TCC (C5b-9) was deposited on both activators, whereas C4b was detected on the ElgM. It is our hope that this method can be applied when studying

complement biosynthesis by cells other than mononuclear phagocytes.

14/3,AB/11 (Item 11 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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6521821 BIOSIS Number: 85122342
INDUCTION OF AN IMMUNE RESPONSE TO A SELF ANTIGEN
STOCKINGER B; HAUSMANN B
BASEL INST. IMMUNOL., 487 GRENZACHERSTR., CH-4005 BASEL, SWITZ.
EUR J IMMUNOL 18 (2). 1988. 249-254. CODEN: EJIMA
Full Journal Title: European Journal of Immunology
Language: ENGLISH

The question has been addressed whether the endogenous B cell population of a mouse can be induced to secrete *antibodies* specific for a self antigen present in serum. The antigen studied was the fifth component of mouse complement (C5). Nude BALB/c mice which are C5 sufficient were used as a source of potentially C5-reactive B cells and endogenous serum C5 provided the antigenic stimulus. We purposely avoided immunization with C5 in adjuvant. T cells from C5-deficient mice which lack this component in serum and are therefore not tolerant of C5 were injected into nude mice as a source of T cell help for *anti*-C5 reactive B cells. Control groups received T cells from C5-sufficient euthymic donors, which are tolerant of C5. Initiation of a response to C5 was monitored by testing the hemolytic function of serum. Reduction of C5-dependent hemolysis was observed in sera of mice which had received T cells from C5-deficient donors. Recipients of T cells from C5-sufficient donors maintained normal hemolytic complement levels throughout the test period of 45 days. Reduction of functional complement levels correlated with the presence of immune complexes of *anti*-C5/C5. C5-specific *antibodies* were mainly IgG1 and carried the IgG1 allotype of BALB/c providing unequivocal evidence that they were derived from the endogeneous B cell population of the C5-sufficient host.

14/3,AB/12 (Item 12 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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6437178 BIOSIS Number: 85037699
ISOLATION PURIFICATION AND *ANTIBODY* PRODUCTION OF HUMAN COMPLEMENT C5
LOU J; JI R; MENG J
SHANGHAI INST. BIOL. PRODUCTS, MINIST. PUBLIC HEALTH, SINO-JAPANESE RES.
CENT. HEMATOL. IMMUNOL.
CHIN J MICROBIOL IMMUNOL (BEIJING) 7 (5). 1987. 328-331. CODEN: ZWMZD
Full Journal Title: Chinese Journal of Microbiology and Immunology
(Beijing)
Language: CHINESE

Using human fresh plasma as source material, C5 was isolated and purified to PAGE pure through PEG precipitation, lysine-Sepharose 4B, DEAE-Sephacel and Sepharose CL-6B chromatography, as well as anti-C3-Sepharose 4B immunoaffinity absorption. This C5 fraction was used directly to immunize rabbits to raise the *anti*-C5 immune serum which was further purified by immunoabsorption with C5 deficient human serum (C5D) to give monospecific antiserum against C5. An in vitro hemolytic system based on the reaction of C5 deficient reagents EAC140xy 23 and C6-9 with test sample, which measured the hemolytic activity of C5 was established and was used in detecting the isolated C5 fractions during column chromatography.

14/3,AB/13 (Item 13 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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6426916 BIOSIS Number: 85027437
FIFTH COMPONENT OF COMPLEMENT C5-DERIVED HIGH-MOLECULAR-WEIGHT MACROPHAGE

CHEMOTACTIC FACTOR IN NORMAL GUINEA-PIG SERUM

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860, JAPAN.

INFLAMMATION 11 (4). 1987. 459-480. CODEN: INFLD

Full Journal Title: Inflammation

Language: ENGLISH

Normal guinea pig serum contain a chemotactic factor(s) for macrophages. As the chemotactic activity in the serum was absorbed by an *anti*-C5* antibody* affinity column but not by the anti-C3 or anti-macrophage chemotactic factor from skin-1 (MCFS-1) affinity column, the major chemotactic factor in the serum was potentiated to be C5-derived. This chemotactic factor, which was a heat-labile molecule with an apparent molecular weight of 150,000 (by gel filtration) and lacked vascular permeability activity, was distinct from the C5a-like anaphylatoxins. Using a combination of a Boyden chamber assay and a morphological polarization assay for the macrophage chemotaxis, it was revealed that this chemotactic factor was latent in plasma and could be activated by incubation for 30 min at 37.degree.C in the presence of a sufficient amount of Ca ion (5 mM) concomitant or not concomitant with the clot formation of the plasma. Precursor of MCFS-1 in plasma was not activated during coagulation.

14/3,AB/14 (Item 14 from file: 55)
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6083581 BIOSIS Number: 34085888

ANTI-C5* MONOCLONAL *ANTIBODIES* INFLUENCE THE HUMAN
MIXED-LEUKOCYTE-REACTION

MONTZ H; ZIERZ R; BIEBER F; SCHULZE M; GOETZE O

ABT. IMMUNOL., GEORG-AUGUST-UNIV. GOETTINGEN, W. GER.

XIXTH MEETING OF THE ASSOCIATION D'IMMUNOLOGIE (SOCIETY OF IMMUNOLOGY),
ULM, WEST GERMANY, OCTOBER 1-3, 1987. IMMUNOBIOLOGY 175 (4). 1987. 268.
CODEN: IMMND

Language: ENGLISH

Document Type: CONFERENCE PAPER

14/3,AB/15 (Item 15 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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6026023 BIOSIS Number: 34028330

INHIBITION OF THE HUMAN MIXED LEUKOCYTE REACTION BY *ANTI*-C5*-C5A
MONOCLONAL *ANTIBODIES*

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ABT. FUER IMMUNOLOGIE, GEORG-AUGUST-UNIVERSITAET, GOETTINGEN, W. GER.

XIITH INTERNATIONAL COMPLEMENT WORKSHOP, CHAMONIX, FRANCE, SEPTEMBER
18-21, 1987. COMPLEMENT 4 (3-4). 1987. 197. CODEN: CMPLD

Language: ENGLISH

Document Type: CONFERENCE PAPER

14/3,AB/16 (Item 16 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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5944780 BIOSIS Number: 84077345

HUMAN ALVEOLAR MACROPHAGES AND MONOCYTES GENERATE THE FUNCTIONAL
CLASSICAL PATHWAY OF COMPLEMENT IN-VITRO

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ACTA PATHOL MICROBIOL IMMUNOL SCAND SECT C IMMUNOL 95 (3). 1987.
117-122. CODEN: APMID

Full Journal Title: Acta Pathologica Microbiologica et Immunologica

Language: ENGLISH

Binding of labelled protein to EIgM kept with macrophage or monocyte cultures with 3H-leucine under serum-free conditions, shows that de novo synthesis of protein with affinity to EIgM takes place. We find that monoclonal anti-C3c and anti-C3g *antibodies* and polyclonal anti-C4 and *anti*-C5 *antibodies* bind to such erythrocytes. This demonstrates that C4b, C3b and iC3b are deposited on the EIgM. Additional evidence for complement synthesis is the increase in binding of anti-C4 *antibodies* to EIgM when the incubation time was increased from 48 to 96 hours. Stimulation of the mononuclear phagocyte cultures with ET was necessary to obtain significant amounts of erythrocyte-bound complement proteins. From these results we conclude that the functional classical pathway of complement is produced in vitro by the monocytes and macrophages.

14/3,AB/17 (Item 17 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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5845672 BIOSIS Number: 83107979

COMPLEMENT COMPONENT C5 IS REQUIRED FOR RELEASE OF ALVEOLAR
MACROPHAGE-DERIVED NEUTROPHIL CHEMOTACTIC ACTIVITY

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NEBR. 68105, USA.

AM REV RESPIR DIS 135 (3). 1987. 659-664. CODEN: ARDSB

Full Journal Title: American Review of Respiratory Disease

Language: ENGLISH

The influx of neutrophils into the alveolar structures can be induced by stimulation of the resistant lung phagocyte, the alveolar macrophage, to release a potent neutrophil chemoattractant(s). We hypothesized that the fifth component of complement (C5) on the cell surface may be required for activation of the alveolar macrophage to release neutrophil chemotactic activity. C5 was identified on guinea pig alveolar macrophages by epifluorescent microscopy, flow cytometry, and enzyme-linked immunoabsorbent assay of eluted macrophages. When cultured for 4 h with stimuli that induce the release of chemotactic activity or for 24 h without added stimuli, purified Fab fragments of a goat *anti*-C5 *antibody* significantly inhibited the ability of macrophages to release chemotactic activity as determined by a blindwell chamber method ($p < 0.001$, all comparisons). This inhibition of chemotactic activity was not detected when *anti*-C5 *antibody* was added after the culture period. In contrast, anti-C3 *antibody* had no inhibitory effect at 4 h or at 24 h ($p > 0.2$, all comparisons). Partial characterization of released chemotactic activity revealed it was of low molecular weight, partially lipid soluble, and not inhibited by C5a chemotactic factor inactivator. These studies suggest that C5 may have a regulatory role in the release of chemotactic activity by alveolar macrophages.

14/3,AB/18 (Item 18 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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5820410 BIOSIS Number: 83082717

ROLE OF CHEMOTACTIC FACTOR INACTIVATOR IN MODULATING ALVEOLAR
MACROPHAGE-DERIVED NEUTROPHIL CHEMOTACTIC ACTIVITY

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I

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J LAB CLIN MED 109 (2). 1987. 164-170. CODEN: JLCMA

Full Journal Title: Journal of Laboratory and Clinical Medicine

Language: ENGLISH

The stimulated alveolar macrophage is a potent source of neutrophil

chemotactic activity. The release of this chemotactic activity can be inhibited by pretreating alveolar macrophages with *anti*-C5* antibody*. We hypothesized that C5a, a fragment cleaved from C5 when C5 is activated, might activate the alveolar macrophage to release neutrophil chemotactic activity and that chemotactic factor inactivator, a serum inhibitor of C5a, could decrease this release. Activated complement components including C5a were found to stimulate guinea pig macrophages to release chemotactic activity into their culture supernatants at levels that were significantly higher than the chemotactic activity of C5a alone ($P < 0.001$). Chemotactic factor inactivator was found to cause a marked reduction in the chemotactic activity released by macrophages stimulated with phagocytic and nonphagocytic stimuli ($P < 0.001$, all comparisons). These data indicate that C5a can stimulate alveolar macrophages to release chemotactic activity in vitro, and that chemotactic factor inactivator may play a role in modulating this process.

14/3,AB/19 (Item 19 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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5771797 BIOSIS Number: 83034104

MICE NATURALLY TOLERANT TO COMPLEMENT C-5 HAVE T CELLS THAT SUPPRESS THE RESPONSE TO THIS ANTIGEN

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EUR J IMMUNOL 16 (10). 1986. 1277-1282. CODEN: EJIMA

Full Journal Title: European Journal of Immunology

Language: ENGLISH

We examined whether C5-sufficient mice which are naturally tolerant to this antigen have suppressor T cells to C5 humoral immune response. Two congenic strains of mice B10.D2 (NSN) and B10.D2 (OSN) differing only in the presence or absence of C5 wer eusd. Irradiated (760 rds) sufficient hosts were reconstituted with a non-adherent spleen cell suspension from either sufficient or deficient mice or a mixture of both. Hemolytic C5 levels were assayed. Sufficient spleen cells appeared to prevent the drop of C5 level caused by *anti*-C5* antibody* made by deficient spleen cells. Spleen cell suspensions from sufficient mice primed with deficient spleen cells exhibited better *anti*-C5* activity than normal sufficient spleen cell suspensions. This *anti*-C5* activity is abrogated by treatment of the NSN spleen cell suspensions obtained from NSN primed with OSN spleen cells with anti-Thy-1.2 antiserum and complement. Suppression of the humoral response to C5 failed to affect the anti-sheep red blood cell immune response. Suppressor T cells are resistant to low-dose irradiation, cortisone treatment and adult thymectomy. In contrast, they are sensitive to high doses of irradiation and both high and low doses of cyclophosphamide treatment. Thus, C5-sufficient mice, in contrast to C5-deficient mice, appear to have antigen-specific suppressor T cells which downregulate the humoral immune response to C5. In addition, we examined the relationship of these suppressor T cells to the state of tolerance in helper T cells of C5-sufficient mice. This was done in irradiated deficient mice which were repopulated with spleen cell suspensions selectively depleted of either Lyt-1+ or Lyt-2+ T cell subsets. These chimeras were challenged with murine C5 and both the primary and secondary immune response was measured by inhibition of the C5 hemolytic activity. It was found that only spleen cell suspensions of the deficient mice selectively depleted from the Lyt-2+ subset of T cells responded to the antigen both in the primary and secondary response. In contrast, either subset of T cells from the sufficient mice failed to respond. Thus, it appears that in sufficient mice helper T cells to C5 are intrinsically tolerant or physically and/or functionally deleted. In conclusion, the data suggest that both T cell compartments are unresponsive and play a role in the mechanism of tolerance to a physiologic antigen.

14/3,AB/20 (Item 20 from file: 55)

5771661 BIOSIS Number: 83033968

SYNTHESIS OF COMPLEMENT C-5 C-6 C-7 C-8 AND C-9 IN-VITRO BY HUMAN
MONOCYTES AND ASSEMBLY OF THE TERMINAL COMPLEMENT COMPLEX

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SCAND J IMMUNOL 24 (4). 1986. 421-428. CODEN: SJIMA

Full Journal Title: Scandinavian Journal of Immunology

Language: ENGLISH

Monocytes cultured under serum-free conditions secreted protein which bound covalently and non-covalently to agarose beads, an activator of the alternative pathway of complement. There was a significant binding of monoclonal anti-C3c *antibodies*, polyclonal *anti*-C5*, anti-C6, anti-C7, anti-C8, and anti-C9 *antibodies*, and of a monoclonal *antibody* against a neoantigen of polymerized C9 to agarose beads incubated with the monocytes for 24, 48, 72 and 96 h. From these results, we conclude that monocytes produce C5, C6, C7, C8 and C9 that assemble as the terminal complement complex on the surface of the agarose beads. Activation by agarose of the alternative pathway with generation to particle bound C3 and C5 convertases is a prerequisite for the subsequent formation of the terminal complement complex. Whether SC5b-9 or the membrane attack of complement (C5b-9) is formed on the beads will be examined.

14/3,AB/21 (Item 21 from file: 55)

DIALOG(R)File 55:BIOSIS PREVIEWS(R)

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5285867 BIOSIS Number: 81053174

INCREASED PLASMA LEVELS OF THE TERMINAL COMPLEMENT COMPLEX IN PATIENTS
WITH EVIDENCE OF COMPLEMENT ACTIVATION

MOLLNES T E; FROLAND S S; HARBOE M

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NORWAY.

COMPLEMENT 2 (2-3). 1985. 175-184. CODEN: CMPLD

Full Journal Title: Complement

Language: ENGLISH

The terminal C5b-9 complex of human complement has recently been described and quantified in normal human plasma by an enzyme-linked immunosorbent assay (ELISA). We collected EDTA plasma samples from 20 patients clinically suspected to have complement activation. The terminal complement complex (TCC) and C3d split products were measured. The TCC was increased in 8 patients, and 6 of these also had increased C3d values, whereas 4 patients had increased C3d and normal TCC values. Two different double-*antibody* assays were used to detect terminal pathway activation: the combination of anti-C6 and *anti*-C5* detecting intermediate complexes as well. There was a close correlation between the observations in these two assays, suggesting that in general the whole cascade including C9 is involved when the terminal pathway of complement is activated in vivo. Quantification of TCC in plasma is an important supplement to already established methods for the evaluation of complement activation in vivo.

14/3,AB/22 (Item 22 from file: 55)

DIALOG(R)File 55:BIOSIS PREVIEWS(R)

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4876432 BIOSIS Number: 80003743

BACTERICIDAL BUT NOT NONBACTERICIDAL C-5B-9 IS ASSOCIATED WITH
DISTINCTIVE OUTER MEMBRANE PROTEINS IN NEISSERIA-GONORRHOEAE

JOINER K A; WARREN K A; HAMMER C; FRANK M M

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INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, BETHESDA, MD 20205.

J IMMUNOL 134 (3). 1985. 1920-1925. CODEN: JOIMA

In this study, the bacterial constituents associated with the complement C5b-9 complex in detergent extracts from serum-treated *N. gonorrhoeae* (GC) were examined. ¹²⁵I surface-labeled GC were incubated in 10% serum, were washed and were solubilized in the zwitterionic sulfo betaine detergent SB12. Immunoprecipitation of ¹²⁵I-GC from the extract with *anti*-C5* Sepharose was followed by 12.5% sodium dodecyl sulfate-polyacrylamide gel electrophoresis autoradiography of immunoprecipitated material. Polyacrylamide gel analysis of surface-labeled ¹²⁵I-GC showed prominent bands for proteins I and III for both serum-resistant GC strain 6305 and serum-sensitive GC strain 7189. These same bands were visible with similar intensity in the SB12 extracts from presensitized and non-presensitized 6305 and 7189 after serum incubation. For those organisms bearing bactericidal C5b-9 (6305 + IgG and 7189 +/- IgG), additional distinctive bands immunoprecipitated with *antibody* to C5 Sepharose. These components were of 93,000, 44,000, 40,000 and 15,000 daltons for 6305 + IgG, and were of 90,000, 50,000, 44,000 and 19,000 daltons for 7189 +/- IgG. Nonbactericidal C5b-9 extracted from the surface of 6305 incubated in serum, but not sensitized with *antibody*, was not associated with these distinctive proteins. This nonbactericidal C5b-9 did have a different pattern of associated bacterial surface constituents from that observed in control samples incubated with *antibody* to human serum albumin, which were similar to those with nonserum-incubated organisms. Evidently, C5b-9 is in a different molecular configuration on the surface of serum-resistant GC from that on the surface of serum-sensitive GC or resistant GC rendered sensitive with bactericidal *antibody*.

14/3,AB/23 (Item 1 from file: 72)

DIALOG(R)File 72:EMBASE

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7720193 EMBASE No: 90148138

Regulation of the human autologous T cell proliferation by endogenously generated C5a

Montz H.; Fuhrmann A.; Schulze M.; Gotze O.

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CELL. IMMUNOL. (USA) , 1990, 127/2 (337-351) CODEN: CLIMB ISSN: 0008-8749

LANGUAGES: English

The immunomodulating role of endogenously synthesized C5 and subsequently generated C5a was studied in a serum-free human autologous mixed leukocyte reaction (AMLR) using either separated T and non-T cell populations or unfractionated mononuclear leukocytes of human peripheral blood. Monoclonal mouse IgG or Fab fragments against human C5/C5a were used as probes for the evaluation of the biological effects of C5a. The reduction of DNA synthesis after the addition of nanogram amounts of *anti*-C5* /C5a mAb was dose-dependent, reaching maximum levels of 30-50%. Of special importance was the availability of a mAb that recognizes a neoepitope present of C5a and not on serum-derived C5. The demonstration of the specificity of its inhibitory effect suggests that C5 is synthesized under the in vitro conditions employed and that the subsequently generated C5a exerts biological effects on T cell proliferation.

14/3,AB/24 (Item 2 from file: 72)

DIALOG(R)File 72:EMBASE

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7552899 EMBASE No: 89275181

Role of C5a in the induction of tumoricidal activity in C3H/HeJ (Lps(d)) and C3H/OuJ (Lps(n)) macrophages

Hogan M.M.; Yancey K.B.; Vogel S.N.

Department of Microbiology, Uniformed Services University of the Health

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J. LEUKOCYTE BIOL. (USA) , 1989, 46/6 (565-570) CODEN: JLBIE ISSN: 0741-5400

LANGUAGES: English

Thioglycollate-elicited macrophages from C3H/HeJ (Lps(d)) and C3H/OuJ (Lps(n)) mice were cultured in a two-signal, tumoricidal assay using recombinant interferon-gamma (rIFN-gamma) as the 'priming' signal and recombinant human C5a (rC5a) as the 'trigger' signal. These experiments were compared directly with a well established, two-signal tumoricidal assay in which rIFN-gamma was used as the 'priming' signal and protein-rich, butanol-extracted lipopolysaccharide (But-LPS) as the 'trigger' signal. These studies showed that rIFN-alpha-primed macrophages can be triggered in a dose-dependent manner by rC5a to effect high levels of tumoricidal activity. Maximum levels of cytotoxicity achieved using this endogenously produced, biologically active peptide as a 'trigger' signal were comparable to those obtained using But-LPS. Moreover, experiments in which *anti*-C5 *antibody* was included in macrophage cultures stimulated with rIFN-gamma and But-LPS showed a significant reduction ($P < .05$) in tumoricidal activity. Because LPS has been shown to induce macrophage C5 production and enzyme release, these findings suggest that macrophage-derived C5 is locally converted to C5a (or some other biologically active C5 cleavage fragment), which functions as an autocrine trigger signal for the induction of tumoricidal activity. In summary, these data suggest 1) that rC5a can provide a 'second signal' to rIFN-gamma-primed murine macrophages for the induction of tumoricidal activity and 2) that macrophage-derived C5 or C5a may represent an autocrine signal induced by exogenous 'trigger signals.'

14/3,AB/25 (Item 3 from file: 72)

DIALOG(R)File 72:EMBASE

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7411214 EMBASE No: 89133448

Binding of complement component C5 to model immune complexes and the use of *anti*-C5 *antibodies* for determination of C5-containing circulating immune complexes

Larsson A.; Sjoquist J.

Department of Medical and Physiological Chemistry, Biomedical Centre, 751 23 Uppsala Sweden

J. CLIN. LAB. IMMUNOL. (United Kingdom) , 1989, 28/1 (5-9) CODEN: JLIMD ISSN: 0141-2760

LANGUAGES: English

When normal human or mouse serum is added to micro ELISA plates coated with monomeric or aggregated IgG, complement component C5 binds to IgG. C5 binding was demonstrated with a specific chicken *anti*-C5 *antibody*. Hydrazine treatment of the serum or addition of EDTA to the serum abolished the binding of C5. C5-deficient mouse serum was negative for C5 binding, whereas the same serum supplemented with human C5 restored the binding of C5. Chicken *anti*-C5 -coated plates were used for determination of C5-containing circulating immune complexes (CIC). Increased concentrations of CIC were found in sera from patients with rheumatoid arthritis and Bell's palsy.

14/3,AB/26 (Item 4 from file: 72)

DIALOG(R)File 72:EMBASE

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7408361 EMBASE No: 89130594

Binding of complement components C1q, C3, C4 and C5 to a model immune complex in ELISA

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J. IMMUNOL. METHODS (Netherlands) , 1989, 119/1 (103-109) CODEN: JIMMB

LANGUAGES: English

When normal human serum is added to microELISA plates coated with monomeric or aggregated IgG various complement components become bound and can be detected with specific chicken anti-Clq, anti-C3, anti-C4 and *anti*-C5* antibodies*. Using such assays we found increased Clq- and decreased C3- and C4-binding in sera from patients with SLE. In contrast, sera from patients with rheumatoid arthritis showed decreased C3 binding but normal Clq binding. The decreases in C3 and C4 binding observed in the sera from patients with SLE were larger than the corresponding decreases determined by radial immunodiffusion. Comparing these results with those of the CH50 assay, the correlation coefficient between CH50 and the C3-binding assay was 0.48. There was no correlation between the results of the CH50 and those of the Clq-, C4- or C5-binding assays.

14/3,AB/27 (Item 5 from file: 72)

DIALOG(R)File 72:EMBASE

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6272162 EMBASE No: 87008787

Synthesis of complement components C5, C6, C7, C8 and C9 in vitro by human monocytes and assembly of the terminal complement complex

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SCAND. J. IMMUNOL. (UK) , 1986, 24/4 (421-428) CODEN: SJIMA

LANGUAGES: ENGLISH

Monocytes cultured under serum-free conditions secreted protein which bound covalently and non-covalently to agarose beads, an activator of the alternative pathway of complement. There was a significant binding of monoclonal anti-C3c *antibodies*, polyclonal *anti*-C5*, anti-C6, anti-C7, anti-C8, and anti-C9 *antibodies*, and of a monoclonal *antibody* against a neoantigen of polymerized C9 to agarose beads incubated with the monocytes for 24, 48, 72 or 96 h. From these results, we conclude that monocytes produce C5, C6, C7, C8 and C9 that assemble as the terminal complement complex on the surface of the agarose beads. Activation by agarose of the alternative pathway with generation of particle bound C3 and C5 convertases is a prerequisite for the subsequent formation of the terminal complement complex. Whether SC5b-9 or the membrane attack of complement (C5b-9) is formed on the beads will be examined.

14/3,AB/28 (Item 6 from file: 72)

DIALOG(R)File 72:EMBASE

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6266764 EMBASE No: 87003389

Mice naturally tolerant to C5 have T cells that suppress the response to this antigen

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EUR. J. IMMUNOL. (GERMANY, WEST) , 1986, 16/10 (1277-1282) CODEN: EJIMA

LANGUAGES: ENGLISH

We examined whether C5-sufficient mice which are naturally tolerant to this antigen have suppressor T cells to C5 humoral immune response. Two congenic strains of mice B10.D2 (NSN) and B10.D2 (OSN) differing only in the presence or absence of C5 were used. Irradiated (760 rds) sufficient hosts were reconstituted with a non-adherent spleen cell suspension from either sufficient or deficient mice or a mixture of both. Hemolytic C5 levels were assayed. Sufficient spleen cells appeared to prevent the drop of C5 level caused by *anti*-C5* *antibody* made by deficient spleen cells. Spleen cell suspensions from sufficient mice primed with deficient spleen cells exhibited better *anti*-C5* activity than normal sufficient spleen cell suspensions. This *anti*-C5* activity is abrogated by treatment of the NSN spleen cell suspensions obtained from NSN primed with OSN spleen cells with anti-Thy-1.2 antiserum and complement. Suppression of

the humoral response to C5 failed to affect the anti-sheep red blood cell immune response. Suppressor T cells are resistant to low-dose irradiation, cortisone treatment and adult thymectomy. In contrast, they are sensitive to high doses of irradiation and both high and low doses of cyclophosphamide treatment. Thus, C5-sufficient mice, in contrast to C5-deficient mice, appear to have antigen-specific suppressor T cells which downregulate the humoral immune response to C5. In addition, we examined the relationship of these suppressor T cells to the state of tolerance in helper T cells of C5-sufficient mice. This was done in irradiated deficient mice which were repopulated with spleen cell suspensions selectively depleted of either Lyt-1sup + or Lyt-2sup + T cell subsets. These chimeras were challenged with murine C5 and both the primary and secondary immune response was measured by inhibition of the C5 hemolytic activity. It was found that only spleen cell suspensions of the deficient mice selectively depleted from the Lyt-2sup + subset of T cells responded to the antigen both in the primary and secondary response. In contrast, either subset of T cells from the sufficient mice failed to respond. Thus, it appears that in sufficient mice helper T cells to C5 are intrinsically tolerant or physically and/or functionally deleted. In conclusion, the data suggest that both T cell compartments are unresponsive and play a role in the mechanism of tolerance to a physiologic antigen.

14/3,AB/29 (Item 7 from file: 72)
DIALOG(R)File 72:EMBASE
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5833451 EMBASE No: 85078961

Bactericidal but not nonbactericidal C5b-9 is associated with distinctive outer membrane proteins in *Neisseria gonorrhoeae*

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J. IMMUNOL. (USA), 1985, 134/3 (1920-1925) CODEN: JOIMA

LANGUAGES: ENGLISH

In this study, we examined the bacterial constituents associated with the complement C5b-9 complex in detergent extracts from serum-treated *Neisseria gonorrhoeae* (GC). sup 1sup 2sup 5I surface-labeled GC were incubated in 10% serum, were washed, and were solubilized in the zwitterionic sulfobetaine detergent SBsub 1sub 2. Immunoprecipitation of sup 1sup 2sup 5I-GC from the extract with *anti*-C5* Sepharose was followed by 12.5% sodium dodecyl sulfate-polyacrylamide gel electrophoresis autoradiography of immunoprecipitated material. Polyacrylamide gel analysis of surgace-labeled sup 1sup 2sup 5I-GC showed prominent bands for proteins I and III for both serum-resistant GC-strain 6305 and serum-sensitive GC strain 7189. These same bands were visible with similar intensity in the SBsub 1sub 2 extracts from presensitized and non-presensitized 6305 and 7189 after serum incubation. For those organisms bearing bactericidal C5b-9 (6305 + IgG and 7189 + or - IgG), additional distinctive bands immunoprecipitated with *antibody* to C5 Sepharose. These components were of 93,000, 44,000 40,000, and 15,000 daltons for 6305 + IgG, and were of 90,000, 50,000, 44,000, and 19,000 daltons for 7189 + or - IgG. Nonbactericidal C5b-9 extracted from the surface of 6305 incubated in serum, but not sensitized with *antibody*, was not associated with these distinctive proteins. However, this nonbactericidal C5b-9 did have a different pattern of associated bacterial surface constituents from that observed in control samples incubated with *antibody* to human serum albumin, which were similar to those with nonserum-incubated organisms. These studies support our earlier experiments which demonstrated that C5b-9 is in a different molecular configuration on the surface of serum-resistant GC from that on the surface of serum-sensitive GC or resistant GC rendered sensitive with bactericidal *antibody*.

14/3,AB/30 (Item 1 from file: 154)
DIALOG(R)File 154:MEDLINE(R)

08585032 93295032

[Neutrophil chemotactic factor in supernatant from pulmonary fibroblasts stimulated with cytokines]

Ogushi F; Masuda M; Fujisawa K; Tani K; Asada K; Yasuoka S; Ogura T

Third Department of Internal Medicine, Tokushima University, Japan.

Nippon Kyobu Shikkan Gakkai Zasshi (JAPAN) Apr 1993, 31 (4) p453-8,

ISSN 0301-1542 Journal Code: KQD

Languages: JAPANESE Summary Languages: ENGLISH

Document type: JOURNAL ARTICLE English Abstract

Fibroblasts are important for maintenance of the structural frame network for most tissues, and they also play an important role in the inflammatory process via production of various mediators. In this study, we demonstrated that pulmonary fibroblasts may participate in pulmonary inflammation by production of neutrophil chemotactic factor (NCF). Pulmonary fibroblasts were stimulated with various cytokines (IGF-1, PDGF, IL-1 alpha, IL-1 beta, IL-2, IL-6, TNF, IFNr). Fibroblasts stimulated with either TNF, IL-1 alpha or IL-beta but not IGF, PDGF, IL-2 or IL-6 demonstrated a kinetic and dose-dependent increase in NCF activity. The NCF activity of crude supernatant was heat-stable and was not changed by *anti*-C5 *antibody* treatment or ether extraction. Characterization of the NCF activity by gel-filtration using high pressure liquid chromatography showed two active fractions, one with MW greater than 100 kD and the other with MW less than 10 kD. NCF activity in the small molecular weight fraction was demonstrated by inhibition of chemotaxis by addition of anti-IL-8 *antibody*. These data suggest that cytokine-treated fibroblast-derived NCF may be important in the pathogenesis and expression of a variety of pulmonary disease processes associated with neutrophil accumulation and activation.

14/3,AB/31 (Item 2 from file: 154)

DIALOG(R)File 154:MEDLINE(R)

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06643271 88288271

Generation of a monoclonal *antibody* to mouse C5 application in an ELISA assay for detection of *anti*-C5 *antibodies*.

Frei Y; Lambris JD; Stockinger B

Basel Institute for Immunology, Switzerland.

Mol Cell Probes (ENGLAND) Jun 1987, 1 (2) p141-9, ISSN 0890-8508

Journal Code: NG9

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We have generated a monoclonal *antibody* with specificity for the fifth component of mouse complement (C5). This *antibody* precipitates the two chains of C5 from normal mouse serum and inhibits C5-dependent hemolysis in a functional complement test. In this study we describe its application in an enzyme-linked immunoadsorbent assay (ELISA assay) for the detection of *anti*-C5 *antibodies* in serum. Monoclonal *anti*-C5 coupled to wells of an ELISA plate specifically binds C5 from unfractionated normal mouse serum. This subsequently serves as antigen to bind *anti*-C5 serum *antibodies*. By this approach we have circumvented the need for extensive purification of C5 from serum which would be required if C5 was directly coupled to ELISA plates as antigen. Serum *antibodies* from C5-immunized mice bound with high avidity to wells containing normal serum as antigen source in amounts representing 1 microgram to 250 ng C5. There was no *antibody* binding to wells containing C5-deficient serum as antigen source. The immune reaction was detected by development with enzyme-coupled goat-anti mouse Ig *antibodies* specific for various mouse Ig subclasses. This method allows the qualitative characterization of immune responses to mouse C5 which is an ideal model for a natural self antigen in studies of immunological tolerance.

14/3,AB/32 (Item 3 from file: 154)

05975678 86276678

The activation of C5 in the fluid phase and in the absence of C3 through the classical pathway of the complement system.

Kitamura H; Tsuboi M; Nagaki K

Immunology (ENGLAND) Jul 1986, 58 (3) p459-65, ISSN 0019-2805

Journal Code: GH7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Unsensitized guinea-pig erythrocytes (Egp) were lysed by a combination of eight isolated, human-derived complement components, C1s, C4, C2, C5, C6, C7, C8 and C9 (C1s-C9exC3), even in the presence of anti-C3. It was determined that a factor was generated in the reaction mixture of C1s, C4, C2, C5 and C6, which had a lytic activity against Egp when C7, C8 and C9 were added. The lytic factor was similar to C56 in the following properties: the activity of the lytic factor decreased when incubated with C7 prior to its reaction with Egp, the lytic factor did not bind to Egp by itself but it did bind in the presence of C7, EDTA did not have any inhibitory effect on the lytic factor, and the activity of the lytic factor was lost by treatment with *anti*-C5* or anti-C6 but not by treatment with anti-C4. Furthermore, C5a, a cleavage product of C5, was clearly detected in the reaction mixture of C1s, C4, C2 and C5. These findings indicate that C5 can be activated proteolytically into C5a and C5b in the fluid phase solely by the classical pathway C3 convertase, C42, without any participation of C3.

14/3,AB/33 (Item 4 from file: 154)

DIALOG(R)File 154:MEDLINE(R)

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05671667 85287667

C56 formation in the reaction mixture of isolated complement components through the classical complement pathway.

Kitamura H; Tsuboi M; Nagaki K

Int Arch Allergy Appl Immunol (SWITZERLAND) 1985, 78 (1) p101-7,

ISSN 0020-5915 Journal Code: GP9

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The mechanism of hemolysis of unsensitized erythrocytes by a mixture of 9 isolated, human-derived complement components, C1s, C4, C2, C3, C5, C6, C7, C8 and C9 (C1s-C9) was studied. Of the tested erythrocytes, guinea pig erythrocytes (Egp) were the most susceptible to lysis by C1s-C9, followed by human and sheep erythrocytes. Contamination of the isolated complement components by C56 was ruled out. It was determined that a factor was generated in the reaction mixture of C1s, C4, C2, C3, C5 and C6 (C1s-C6), which had lytic activity against Egp when C7, C8 and C9 were added. We found that the lytic factor was similar to C56 in the following properties: (1) the activity of the lytic factor decreased when incubated with isolated C7 prior to its reaction with Egp; (2) the lytic factor did not bind to Egp by itself but it did bind in the presence of C7; (3) EDTA did not have any inhibitory effect on the lytic factor; (4) the activity of the lytic factor decreased by treatment with *anti*-C5* and anti-C6 but not by treatment with anti-C3 and anti-C4, and (5) gel filtration of the reaction mixture (C1s-C6) indicated that the elution volumes of the lytic factor and of isolated C56 were similar. Thus, it is likely that C56 is generated in the reaction mixture of C1s-C6 and the lytic factor binds to unsensitized erythrocytes together with C7, to form an intermediate EC567 which is susceptible to lysis by the action of C8 and C9.

Processing

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22/3,AB/1 (Item 1 from file: 55)

DIALOG(R)File 55:BIOSIS PREVIEWS(R)

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11226831 BIOSIS Number: 97426831

C5b-9 increases albumin permeability of isolated glomeruli in vitro
Savin V J; Johnson R J; Couser W G
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Kidney International 46 (2). 1994. 382-387.

Full Journal Title: Kidney International

ISSN: 0085-2538

Language: ENGLISH

Deposition of *antibody* and activation of the complement cascade are important in both naturally occurring *glomerulonephritis* and in experimental models including passive Heymann *nephritis*. We studied the effect of *antibody* and complement on albumin permeability of isolated glomeruli to determine the role of the terminal complement components (C5-C9) in mediating the proteinuria in *nephritis*. Isolated glomeruli were *treated* with anti-Fx1a (Heymann *antibody*) and then incubated them with pooled human serum, serum in which complement had been inactivated by heat, or serum deficient in C6 or C7. The albumin reflection coefficient (sigma-albumin) was calculated from the volumetric response of glomeruli to transcapillary oncotic gradients produced by albumin or high molecular weight neutral dextran (252 kD). Convectional permeability to albumin (P-albumin) was calculated as 1-sigma-albumin. Albumin permeability of control glomeruli was not different from 0. Albumin permeability was not altered by *antibody* alone but was increased to 0.65 +/- 0.04 when *antibody* *treated* glomeruli were incubated for 10 minutes with pooled serum as a source of complement. Heat *treatment* of serum to inactivate

- Claims
complem. components

complement prevented the increase in permeability. Incubation for 10 minutes with serum without *antibody* pretreatment caused a lesser increase in permeability of isolated glomeruli (0.18 +- 0.06). Serum deficient in either C6 or C7 did not cause an increase in albumin permeability of *antibody* pre-*treated* glomeruli, but incubation with a combination of these sera (now containing the complete cascade) increased permeability to the same extent as did pooled normal serum (0.58 +- 0.04). We conclude that activation of the terminal complement components is required for the increase in glomerular macromolecular permeability caused by anti-Fx1a and that terminal complement activation is sufficient to alter the permeability independent of complement hemodynamic events or contribution by circulating cells.

22/3,AB/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11114260 BIOSIS Number: 97314260

Bromophenacyl bromide binding to the actin-bundling protein l-plastin inhibits inositol trisphosphate-independent increase in Ca-2+ in human neutrophils

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Proceedings of the National Academy of Sciences of the United States of America 91 (9). 1994. 3534-3538.

Full Journal Title: Proceedings of the National Academy of Sciences of the United States of America

ISSN: 0027-8424

Language: ENGLISH

Ligation of IgG Fc receptors on polymorphonuclear leukocytes causes an increase in the concentration of free intracytoplasmic Ca-2+ ((Ca-2+)-i) which arises from release of intracellular stores but is independent of inositol 1,4,5-trisphosphate. We found that bromophenacyl bromide (BPB), an alkylating agent which inhibits leukocyte degranulation, adherence, and phagocytosis, inhibited IgG-stimulated increases in (Ca-2+)-i with an IC-50 of 0.2 mu-M. In contrast, BPB had no effect on inositol 1,4,5-trisphosphate-dependent (Ca-2+), increases induced by fMet-Leu-Phe, complement fragment *C5a* , ATP, or platelet-activating factor. Using a monoclonal *antibody* specific for BPB, we identified in polymorphonuclear leukocytes a single cytosolic protein of 66 kDa and isoelectric point pH 5.6 which bound BPB when intact cells were *treated* with the alkylating agent. This BPB-binding protein was identified as l-plastin, a Ca-2+-regulated actin-bundling protein. l-Plastin was found associated with the Triton X-100-insoluble cytoskeleton in polymorphonuclear leukocytes adherent to *immune* *complexes* , suggesting that BPB affects Fc receptor-mediated signal transduction by altering the actin cytoskeleton. Consistent with this hypothesis, both cytochalasin B and cytochalasin D inhibited the IgG-dependent increase in (Ca-2+)-i, without any effect on fMet-Leu-Phe-induced Ca-2+ release. These data suggest that the actin cytoskeleton is essential for signal transduction from plasma membrane Fc receptors and that l-plastin has a critical role in activation of this pathway.

22/3,AB/3 (Item 3 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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10054126 BIOSIS Number: 95054126

NPC 15669 INHIBITS THE REVERSED PASSIVE ARTHUS REACTION IN RATS BY BLOCKING NEUTROPHIL RECRUITMENT

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J PHARMACOL EXP THER 263 (3). 1992. 933-937. CODEN: JPETA

Full Journal Title: Journal of Pharmacology and Experimental Therapeutics

Language: ENGLISH

NPC 15669, N-carboxyl-L-leucine, N-[(2,7-dimethylfluoren-9-yl)methyl]ester, has been shown to inhibit several inflammatory reactions that depend upon recruitment of neutrophils into the primary lesion. In the present study we examined the effects of NPC 15669 in the reversed passive Arthus reaction, an inflammatory reaction occurring in the skin of rats in response to intracutaneous injection of antigen followed by intravenous administration of *antibody*. In this model, *immune* *complex* formation activates complement, resulting in rapid recruitment of neutrophils to the site, which releases free radicals and proteases that damage capillaries, resulting in plasma leak. NPC 15669 inhibited the increased capillary permeability occurring in the reversed passive Arthus reaction in a dose-dependent manner, with an ED50 of 4 mg/kg. The agent similarly inhibited the recruitment of radiolabelled neutrophils as well as accumulation of myeloperoxidase, a neutrophil marker, NPC 15669 in vitro inhibited the adherence of formyl-L-Met-L-Leu-L-Phe- or human recombinant *C5a*-activated neutrophils to endothelium, with IC50 values of 15 to .mu.M (ca. 4-9 .mu.g/ml). Measurement of plasma NPC 15669 showed that at the ED50 dose, the average circulating concentration of drug was 5 .mu.g/ml, consistent with the hypothesis that NPC 15669 exerts its anti-inflammatory effects by inhibiting neutrophil adherence to endothelium and recruitment into the inflammatory lesion.

22/3,AB/4 (Item 4 from file: 55)

DIALOG(R)File 55:BIOSIS PREVIEWS(R)

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9507140 BIOSIS Number: 94012140

ACUTE EFFECT OF PASSIVE HEYMANN *NEPHRITIS* ON RENAL BLOODFLOW AND GLOMERULAR FILTRATION RATE IN THE RAT ROLE OF THE ANAPHYLATOXIN *C5A* AND THE ALPHA-ADRENERGIC NERVOUS SYSTEM

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NEPHRON 60 (4). 1992. 453-459. CODEN: NPRNA

Full Journal Title: Nephron

Language: ENGLISH

In earlier studies, we have shown that induction of passive Heymann *nephritis* (PHN) by intrarenal infusion of anti-Fx1A *antibodies* provokes an immediate fall in renal blood flow (RBF) and glomerular filtration rate (GFR). This was probably mediated via the complement system, as infusion of the F(ab')₂ fraction of anti-Fx1A did not reduce RBF and GFR. In the present study, the effects of .alpha.-adrenergic blockade upon the acute hemodynamic changes during induction of PHN and of *C5a* infusion were studied. Group 1 was infused with anti-Fx1A *antibodies* during blockade of the sympathetic nervous system with the .alpha.-blocker phentolamine; control animals were *treated* similarly, but infused with normal rat IgG. Group 2 was infused with the anaphylatoxin *C5a*, normally produced during complement activation, and compared with control animals infused with saline. In group 1, RBF did not differ from control animals after the infusion of anti-Fx1A *antibodies* (6.6 +/- 0.5 compared to 7.3 +/- 1.0 ml/min/g in the controls). GFR in the left, *antibody*-infused kidney fell compared to controls, and was 0.25 +/- 0.08 ml/min/g at the end of the experiment compared to 0.60 +/- 0.13 ml/min/g (p < 0.05 with Student's t test, p = 0.07 with two-way analysis of variance (ANOVA). GFR in the right kidney remained unchanged compared to controls. In group 2, *C5a* induced a significant fall in RBF (from 7.9 +/- 0.9 to 3.1 +/- 0.4 ml/min/g kidney weight), significantly different from control animals where it fell from 8.1 +/- 0.5 to 6.8 +/- 0.7 ml/min/g (p < 0.0001 with two-way ANOVA, p < 0.001 with t test). GFR did not differ significantly from control animals. These results indicate that both the sympathetic nervous system and the anaphylatoxin *C5a* are mediators of acute hemodynamic changes in PHN.

22/3,AB/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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9038760 BIOSIS Number: 93023760

C6 DEPLETION REDUCES PROTEINURIA IN EXPERIMENTAL NEPHROPATHY INDUCED BY A
NONGLOMERULAR ANTIGEN

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J AM SOC NEPHROL 2 (4). 1991. 894-901. CODEN: JASNE

Language: ENGLISH

The role of the complement membrane attack complex, *C5b*-9, in mediating glomerular injury has been well defined in models of membranous nephropathy induced by *antibody* to endogenous glomerular epithelial cell membrane antigens. The effect of selective C6 depletion (to prevent *C5b*-9 formation) on morphologic characteristics and proteinuria in a model of *in situ* subepithelial *immune* *complex* *nephritis* induced by an exogenous cationized antigen (human immunoglobulin G (IgG)) followed by rabbit *antibody* to human IgG was studied. Selective C6 depletion was achieved by repeated administration of a goat *antibody* to rat C6. Other groups were *treated* with cobra venom factor to induce generalized complement depletion and with sublethal irradiation to deplete circulating leukocytes. In C6 depleted rats, C6 levels were reduced to less than 3% of baseline throughout the 2 days of the study compared with over 100% in controls. At 4 h after disease induction, glomerular deposition of antigen and *antibody* were similar in C6D and control groups by immunofluorescence and by direct measurement of glomerular deposition of radiolabeled antigen and *antibody* (cationized 131I-human IgG, 9.1 \pm 0.1 μ g/38,000 glomeruli in C6D versus 9.8 \pm 0.9 in controls; P = was not significant; rabbit 125I-labeled anti-human IgG, 104 \pm 10 ng in C6D versus 80 \pm 9 ng in controls; P = was not significant). Circulating C3 levels and glomerular C3 deposition were also similar in C6D and control groups. Proteinuria in C6D rats was reduced compared with controls 0 to 24 h after disease induction (8.5 \pm 1 mg/day in C6D versus 45 \pm 25 in controls; P < 0.05) and 24 to 48 h after disease induction (35 \pm 5 in C6D versus 65 \pm 10 in controls; P < 0.05). Generalized complement depletion reduced proteinuria to baseline levels on both day 1 and day 2, whereas leukocyte depletion produced a significant reduction in proteinuria only on day 2. The results demonstrate that *C5b*-9 is a major mediator of glomerular injury in a model of *immune* *complex* *nephritis* induced with a nonglomerular antigen.

22/3,AB/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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6658265 BIOSIS Number: 86124816

ENDOTOXIN-INDUCED AUTO-IMMUNITY IN MICE II. REACTIVITY OF
LPS-HYPORESponsive AND C5-DEFICIENT ANIMALS

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INT ARCH ALLERGY APPL IMMUNOL 86 (4). 1988. 370-374. CODEN: IAAAA

Full Journal Title: International Archives of Allergy and Applied
Immunology

Language: ENGLISH

Auto-*antibody* responses and circulating *immune* *complex* levels of mice with abnormal reactions to endotoxin were investigated after injection with the bacterial product. It was observed that C3H/HeJ mice displayed very high background plaque-forming cell responses towards bromelain-*treated* isologous erythrocytes which were slightly enhanced by endotoxin *treatment*. The same animals, however, did not bear autohaemolysins in

their serum, but became so upon endotoxin injection. A possible relationship between the high background reactivity of C3H/HeJ mice and the low toxicity of endotoxin in these animals is discussed. Neither untreated nor lipopolysaccharide-injected C3H/HeJ mice showed significant *immune* *complex* levels in their sera. This may be explained by their hyporesponsiveness, but by a low sensitivity to the toxic effects of endotoxin as well. C5-deficient and C5-sufficient mice showed similar auto-immune reactions, indicating that *C5a*, which is responsible for other effects of endotoxin, is not involved in endotoxin-induced auto-immunity.

22/3,AB/7 (Item 7 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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6437233 BIOSIS Number: 85037754

FUNCTIONAL HETEROGENEITY OF *IMMUNE* *COMPLEXES* IN EPIDERMOLYSIS BULLOSA ACQUISITA

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J INVEST DERMATOL 89 (5). 1987. 478-483. CODEN: JIDEA

Full Journal Title: Journal of Investigative Dermatology

Language: ENGLISH

Epidermolysis bullosa acquisita is an inflammatory subepidermal bullous disease characterized by circulating and tissue-bound complement-binding anti-basement membrane zone autoantibodies to type VII procollagen. Lesions are characterized by neutrophil-predominant inflammation in some patients, but not in others. These features suggest complement activation and generation of complement-derived chemotactic factors for leukocytes by basement membrane zone *immune* *complexes* may contribute to inflammation, but that complexes may be heterogeneous in the ability to express that function. In this study, we measured the ability of basement membrane zone complexes from patients with (n = 4) and without (n = 6) neutrophil predominant inflammation to activate complement and generate complement-derived chemotactic activity using a complement-dependent neutrophil attachment assay. The results showed considerable heterogeneity in neutrophil attachment among EBA patients and that both the incidence (4/4 vs 2/6) and magnitude (81 \pm 34 vs 12 \pm 10 neutrophils/mm basement membrane zone) of attachment were greater in patients with neutrophil-predominant inflammation. Functional heterogeneity appeared to be due to differences in the amounts of complement-activating complexes formed at the basement membrane zone, which in turn appeared to be due to differences in the availability of circulating complement-binding anti-basement membrane zone *antibodies*. This was suggested by a positive correlation ($r = 0.72$, $p < 0.01$) between neutrophil attachment and complement-binding anti-basement membrane zone antibody titers and the observation that high levels of neutrophil attachment could be generated in skin from patients with epidermolysis bullosa acquisita who did not have neutrophil-predominant inflammation by *treating* their skin in vitro with complement-binding anti-basement membrane zone *antibodies*. These results suggest tissue complexes in epidermolysis bullosa acquisita are heterogeneous in the ability to activate complement and generate complement-derived chemotactins (*C5a*, *C5a* des arg), and that functional heterogeneity contributes to histologic heterogeneity. The functional immunologic-pathologic correlation observed in this study suggest epidermolysis bullosa acquisita is an autoimmune "collagen" disease.

22/3,AB/8 (Item 8 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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5813695 BIOSIS Number: 83076002

PSYCHOPHARMACOLOGICAL ACTIVITY OF *IMMUNE* *COMPLEXES* IN RAT BRAIN IS

COMPLEMENT DEPENDENT

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J NEUROIMMUNOL 13 (3). 1987. 293-304. CODEN: JNRID

Full Journal Title: Journal of Neuroimmunology

Language: ENGLISH

Sprague-Dawley male rats implanted with chronic indwelling cannulae at the perifornical hypothalamus eat excessively during the sixth hour following administration of exogenous *immune*-complexing* reactants to the brain site. Rabbit anti-HSA was injected, followed in 30 min by a 20-fold excess of antigen. Anaphylatoxin *C5a* has also been shown to induce excessive intake, an effect similar to that of norepinephrine at this brain site. If the anaphylatoxins or other byproducts or consequence of the complement cascade were responsible for the *immune* *complex* effect, interference with the initiation of the cascade or with the conversion of C3 to C3a and C3b should abolish the behavioral response. These experiments demonstrate that *immune* *complexes* formed with the non-complement-fixing F(ab')₂ fragment of the rabbit anti-HSA do not induce eating, and that normally active IgG *antibody* complexes do not induce eating if the site has been pretreated with goat anti-rat C3. This latter *treatment* had no effect, however, on the ability of the animals to respond to norepinephrine or to *C5a*. We conclude that the *immune* *complex* effect is complement dependent.

22/3,AB/9 (Item 1 from file: 72)

DIALOG(R)File 72:EMBASE

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8999320 EMBASE No: 93303037

Mediation of immune glomerular injury

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CLIN. INVEST. (Germany), 1993, 71/10 (808-811) CODEN: CINVE ISSN: 0941-0198 ADONIS ORDER NUMBER: 094101989300149N

LANGUAGES: English SUMMARY LANGUAGES: English

Although glomerular disease remains the most common cause of end-stage renal disease worldwide, major advances have been made recently in understanding the cellular and molecular mechanisms which mediate these disorders. Nephrotic syndrome in non inflammatory lesions such as minimal-change/focal sclerosis and MN results from disorders of the GEC which can be simulated in animal models by *antibodies* to various GEC membrane epitopes. Clarification of how these *antibodies* effect the GEC to induce a loss of glomerular barrier function should substantially improve understanding of the pathogenesis of minimal change/focal sclerosis. In MN, proteinuria is mediated primarily by *C5b*-9 through similar mechanisms that also involve the GEC as a target. Inflammatory glomerular lesions are induced by circulating inflammatory cells or proliferating resident glomerular cells. Understanding of how these cells induce tissue injury has also evolved considerably over the past decade. Neutrophil-induced disease involves leukocyte adhesion molecules in regulating neutrophil localization; proteases, oxidants, and myeloperoxidase in mediating injury and platelets in augmenting these processes. The activated mesangial cell exhibits altered phenotype and proliferation with release of oxidants and proteases. Mesangial cell proliferation may be initiated by basic fibroblast growth factor and is maintained by an autocrine mechanism involving PDGF. TGF-beta is important in the subsequent development of sclerosis. As understanding of these areas evolves, numerous new *therapeutic* strategies can now be devised, including agents which block or inhibit complement effects, oxidants, proteases, growth factors, and other cytokines. Appreciation of the role of several natural inhibitors of these mechanisms may also allow *therapeutic* manipulations that upregulate regulatory proteins, with a consequent *therapeutic* benefit. Thus these changes in basic understanding of the mechanisms of glomerular disease are likely to translate into new and more

specific and effective forms of *therapy* in the next decade.

22/3,AB/10 (Item 2 from file: 72)
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8730002 EMBASE No: 93033947

Acute renal failure and degenerative tubular lesions associated with in situ formation of adenovirus *immune* *complexes* in a patient with allogeneic bone marrow transplantation

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TRANSPLANTATION (USA) , 1993, 55/1 (67-72) CODEN: TRPLA ISSN: 0041-1337

LANGUAGES: English SUMMARY LANGUAGES: English

We describe the development of acute renal failure and degenerative tubular lesions associated with local immune deposits in a patient with allogeneic bone marrow transplantation. A 21-year-old man with an acute myelocytic leukemia received a bone marrow graft from a cousin mismatched for a single HLA-DR locus antigen. Hemorrhagic cystitis due to adenovirus type 11 infection occurred 26 days after transplantation, and 17 days later the patient developed acute renal failure. A study of renal tissue obtained by needle biopsy showed degenerative and necrotic lesions, especially in the distal part of the nephron. By electron microscopy adenovirus type 11 particles were found in the nuclei of tubular cells and in cellular debris in tubular lumina. By immunofluorescence technique, granular immune deposits containing adenovirus type 11 related antigen(s), immunoglobulins, C3, and membrane attack complex (MAC) *C5b*-9 of the complement system were detected along the tubular basement membranes but not in glomeruli. The patient's IgG did not bind to normal human kidneys. These findings suggest that adenovirus type 11 directly induced acute tubular damage, and that the tubular immune deposits were formed 'in situ' by viral antigens and circulating viral *antibody*.

22/3,AB/11 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE
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7697785 EMBASE No: 90128948

Critical notes on recent progress in nephrology

NEFROLOGIA

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MED. RIV. ENCICL. MED. ITAL. (Italy) , 1989, 9/4 (467-474) CODEN: MEDIE
ISSN: 0392-6516

LANGUAGES: Italian SUMMARY LANGUAGES: English

Advances in biomedical technology have contributed effectively to the resolution of basic and clinical problems in Nephrology. Most of our insights on glomerular diseases come from animal models. *Antibodies* against components of the extracellular matrix have been shown to induce glomerular changes in vivo and the non-collagenous NC1 domain of type IV collagen has been demonstrated to contain the Good pasture antigen. New pathogenetic mechanisms of glomerular injury are suggested by studies on the interaction of *antibodies* with glomerular cell surface antigens. Gp330, a glycoprotein expressed at the surface of glomerular visceral epithelial cells, has been recognized to be the most relevant antigen of Heymann *nephritis*. *Antibodies* able to crosslink gp330 bind to the antigen at the base of foot processes and the resulting *immune* *complexes* are shed into the subepithelial space where they form electron dense deposits. The complement membrane attack complex (*C5b*-9) is likely to be directly responsible for epithelial cell injury and proteinuria in

this model. Other cell surface antigens of the glomerular capillary wall, such as dipeptidyl dipeptidase IV, podocalyxin, podocin, have been characterized. A novel model of glomerular injury comes from the demonstration that a non-complement fixing monoclonal *antibody* to a surface sialo-glycoprotein (SGP-115/107) binds to glomerular visceral epithelial cells and causes morphological changes which appear epitopespecific and complement and leukocyte-independent. The mechanisms responsible for the progression of renal disease to glomerular sclerosis have been extensively explored in the last years. Among the hemodynamic factors intraglomerular hypertension has been established to play an important part, at least in some models. Recent studies have emphasized the role of alternative mechanisms, such as glomeruli and interstitium. Our knowledge of the mediators of glomerular injury is markedly expanding. Products released by leukocytes, platelets, and intrinsic glomerular cells exert direct and indirect effects on the kidney, and the pharmacological inhibition of some of them, such as free oxygen radicals, thromboxane A₂, LTD₄, platelet activating factor, has been shown to attenuate structural and functional changes in experimental models of renal diseases. Only recently peptide growth factors, cytokines, and endothelin have been recognized to influence functions of renal cells in vitro and in vivo. The role of the cellular immunity and the expression of major histocompatibility antigens have also been studied both in *glomerulonephritis* and in tubular-interstitial nephropathies. Interesting progress has recently been made in understanding the pathogenesis of some genetic disease, of the kidney. Using in vitro cultures of renal tissues and techniques of molecular biology it has been established the importance of the altered remodeling of extracellular matrix in the genesis of the renal cysts. The production of human recombinant erythropoietin is a fundamental contribution of molecular biology to the management of uremia and probably to the knowledge of its pathophysiology. However, the significance of some undesired effects of this peptide has yet to be elucidated. The case of cyclosporine nephrotoxicity is a remarkable example of long term effects of a chronic *therapy*. Important studies have documented the risk of loss of renal function in patients with cardiac transplantation *treated* with cyclosporine. Another new clinical condition capable to cause the deterioration of renal function is the HIV-associated nephropathy, whose pathological pattern might elicit the suspect of AIDS in patients at risk.

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7155179 EMBASE No: 88151453

Rapidly progressive *glomerulonephritis*: Classification, pathogenetic mechanisms, and *therapy*

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AM. J. KIDNEY DIS. (USA), 1988, 11/6 (449-464) CODEN: AJKDD ISSN: 0272-6386

LANGUAGES: English

Immunopathologic studies over the past two decades have demonstrated that rapidly progressive *glomerulonephritis* (RPGN) can result from glomerular deposition of anti-GBM *antibody*, *immuno* *complexes*, or from some as yet undefined mechanism that does not involve glomerular *antibody* deposition. The latter process may be cell mediated and resembles a small vessel vasculitis. Most cases of idiopathic RPGN are not accompanied by pathogenic glomerular immunoglobulin deposition. Recent experimental studies of immune mechanisms of glomerular injury have identified several new processes that can induce damage to the capillary wall sufficient to result in crescentic *glomerulonephritis* (GN). These include direct effects of anti-GBM *antibody* alone and of the complement *C5b*⁻⁹ (membrane attack) complex, *nephritogenic* effects of inflammatory effector cells that involve reactive oxygen species and glomerular halogenation, and

injury mediated by sensitized lymphocytes independently of *antibody* deposition. Macrophages have been shown to participate in both intracapillary and extracapillary fibrin deposition and crescent formation as well as to mediate capillary wall damage. The role of resident glomerular cells and cell-cell interactions in *glomerulonephritis* is still under active investigation. Despite these several advances in understanding immune injury to the glomerulus, *therapy* for RPGN remains largely empiric. Although the prognosis in RPGN has clearly improved over time, no form of disease-specific *therapy* has been clearly shown yet to be beneficial in a controlled study. Interpretation of the existing literature on *therapy* is complicated by the availability of only historical rather than concurrent controls, lack of attention to several variables known to affect disease outcome, and uncertainty regarding bias in favor of reporting positive results. Available data suggests that optimal outcomes may be achieved in anti-GBM *nephritis* by *treatment* with steroids, immunosuppression and plasma exchange, particularly when *therapy* is directed at patients with mild but rapidly progressive disease before oliguria or severe azotemia develop. Pulse steroids are probably the most cost-effective *therapy* for the idiopathic form of RPGN, but *treatment* with cytotoxic agents should be considered if clinical or histologic evidence of vasculitis is present.

22/3,AB/13 (Item 5 from file: 72)
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7005173 EMBASE No: 88006482

Immune *complex* ' mediated intravascular hemolysis due to IgM cephalosporin-dependent *antibody*

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TRANSFUSION (PHILADELPHIA) (USA) , 1987, 27/6 (460-463) CODEN: TRANA

ISSN: 0041-1132

LANGUAGES: English

Immune hemolytic anemia (IHA) related to cephalosporins is rare and generally considered to be the result of a drug-adsorption mechanism. In previously reported cases, the hemolysis was usually extravascular and the causative *antibodies* were IgG, incapable of activating complement, and demonstrable by the direct or indirect antiglobulin test using red cells (RBCs) pretreated in vitro with cephalosporin. The authors report a patient in whom acute intravascular hemolysis developed while she was receiving cefotaxime (a cephalosporin as yet not reported to cause IHA). The patient's RBCs were coated only with complement fragments (C3d), even at the peak of the hemolytic episode. Her serum and eluates repeatedly yielded negative results when tested against normal or cephalosporin-coated RBCs. However, strong hemagglutination and *C5b* -9-mediated hemolysis were observed if the patient's serum was tested against RBCs in the presence of the drug, its ex vivo antigen and, to a lesser degree, cephalothin and ceftriaxon, but not in the presence of penicillin and other related cephalosporins. The positive reactions were not changed by preincubating the serum with different amounts of the drugs. All of these findings reflect the typical picture of drug-induced IHA by the so-called '*immune* *complex*' mechanism and not by the drug-adsorption mechanism. The authors conclude that cephalosporin can cause immune hemolysis in two ways: the drug-adsorption mechanism and, as described here, the '*immune* *complex*' mechanism.

22/3,AB/14 (Item 6 from file: 72)
DIALOG(R)File 72:EMBASE
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6203065 EMBASE No: 86198126

Mechanism by which methylprednisolone inhibits acute *immune* *complex*

-induced changes in vascular permeability
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Louisville, KY 40292 USA
INFLAMMATION (USA) , 1986, 10/3 (321-332) CODEN: INFLD
LANGUAGES: ENGLISH

Intravital microscopy was used to quantitate protein leakage which resulted from the deposition of *immune* *complexes* in the vasculature of the rat cremaster muscle. *Immune* *complex* deposition was initiated by the addition of 80 mug/ml of ovalbumin to the bath surrounding the muscle, followed by the intravenous administration of antiovalbumin. Administration of 25 mg/kg of antiovalbumin produced significant leakage of protein from the third-order venules, while 7.5 and 2.5 mg/kg had no effect. Administration of methylprednisolone (MP), 30 mg/kg, 1 h prior to the deposition of *immune* *complexes* significantly inhibited protein leakage. In separate experiments, MP inhibited intradermal edema formation and protein exudation induced in rats by histamine, platelet activating factor, or *C5a*. However, MP had no effect on protein exudation or edema produced by xanthine oxidase or glucose oxidase. Intravenous administration of MP inhibited the ability of polymorphonuclear leukocytes (PMNs) to phagocytize bacteria, but failed to alter hydrogen peroxide production. These results suggest that MP prevents acute changes in vascular permeability following *immune* *complex* deposition by inhibiting the effects of soluble mediators of edema on vascular endothelium and by inhibiting PMN phagocytosis.

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08763797 94078797
Current topics in childhood lupus *nephritis*.
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Acta Paediatr Jpn (AUSTRALIA) Oct 1993, 35 (5) p480-7, ISSN 0374-5600
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Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Lupus *nephritis* is a major predictor of the prognosis of systemic lupus erythematosus (SLE). The present paper discusses lupus *nephritis* from clinical and immunopathological points of view. Although recent advances in diagnosis and *treatment* improve the prognosis of children with SLE, there remain many unsolved clinical problems. One of the current topics in the *treatment* for SLE is intermittent intravenous cyclophosphamide *therapy* which is effective even for the steroid-resistant patients with severe lupus *nephritis* , at least for short-term observation. Immunopathologically, the following issues are discussed: (i) The *C5b*-9 terminal complement complex plays an important role in the pathogenesis of lupus *nephritis*. The possible interaction of vitronectin and SP-40,40 is also mentioned; (ii) A semi-quantitative analysis of the charge barrier of the glomerular basement membrane reveals that the charge barrier dysfunction plays an important role in the pathogenesis of proteinuria in lupus *nephritis* . This study also demonstrates that the charge of immune deposits is important for the initiation of glomerular injury in lupus *nephritis* ; (iii) It is demonstrated that the histopathological diversity of lupus *nephritis* is based on biological properties of *nephritogenic* auto-*antibodies* in murine lupus models.

22/3,AB/16 (Item 2 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
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07584255 91103255
Urinary excretion of the *C5b*-9 membrane attack complex of complement is

a marker of immune disease activity in autologous *immune* *complex*
nephritis.

Pruchno CJ; Burns MM; Schulze M; Johnson RJ; Baker PJ; Alpers CE; Couser
WG

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Am J Pathol (UNITED STATES) Jan 1991, 138 (1) p203-11, ISSN 0002-9440
Journal Code: 3RS

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DK, NIDDK

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The urinary excretion of the *C5b* -9 membrane attack complex of complement correlates with glomerular deposition of *antibody* in the passive Heymann *nephritis* (PHN) model of membranous nephropathy (MN). To determine if this parameter can be correlated with *antibody* deposition in a model of MN induced by an autologous mechanism and thus more analogous to human MN, the relationship of urinary *C5b* -9 to ongoing glomerular *immune* *complex* formation late in autologous *immune* *complex* *nephritis* (AICN) was studied. Based on urinary *C5b* -9, the animals were divided into two groups at 12 weeks after induction of AICN, those with persistently high urinary *C5b* -9 excretion and those in whom urinary excretion of *C5b* -9 returned to undetectable levels. While all rats developed glomerular deposition of rat IgG and significant proteinuria, high *C5b* -9 excretors had greater proteinuria and prolonged positive staining for glomerular C3. When normal syngeneic kidneys were transplanted into rats (n = 3) from each group, only those with persistent *C5b* -9 excretion developed subepithelial immune deposits of rat IgG in the transplanted kidney. As in the PHN model of MN, proteinuria was dissociated widely from urinary *C5b* -9 excretion, glomerular C3 staining, and evidence of circulating *antibody*. Thus these findings demonstrate that urinary excretion of *C5b* -9 serves as an index of on-going immunologic disease activity in the AICN model of MN, while proteinuria does not.

22/3,AB/17 (Item 3 from file: 154)

DIALOG(R)File 154:MEDLINE(R)

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07324080 90231080

[Nephrology]

Nefrologia.

Abbate M; Remuzzi G

Medicina (Firenze) (ITALY) Oct-Dec 1989, 9 (4) p467-74, ISSN
0392-6516 Journal Code: MEE

Languages: ITALIAN Summary Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL English
Abstract

Advances in biomedical technology have contributed effectively to the resolution of basic and clinical problems in Nephrology. Most of our insights on glomerular diseases come from animal models. *Antibodies* against components of the extracellular matrix have been shown to induce glomerular changes in vivo and the non-collagenous NC1 domain of type IV collagen has been demonstrated to contain the Goodpasture antigen. New pathogenetic mechanisms of glomerular injury are suggested by studies on the interaction of *antibodies* with glomerular cell surface antigens. Gp330, a glycoprotein expressed at the surface of glomerular visceral epithelial cells, has been recognized to be the most relevant antigen of Heymann *nephritis*. *Antibodies* able to crosslink gp330 bind to the antigen at the base of foot processes and the resulting *immune* *complexes* are shed into the subepithelial space where they form electron dense deposits. The complement membrane attack complex (*C5b* -9) is likely to be directly responsible for epithelial cell injury and proteinuria in this model. Other cell surface antigens of the glomerular capillary wall, such as dipeptidyl dipeptidase IV, podocalyxin, podoendin, have been characterized. A novel model of glomerular injury comes from the demonstration that a non-complement fixing monoclonal *antibody* to a

surface sialo-glycoprotein (SGP-115/107) binds to glomerular visceral epithelial cells and causes morphological changes which appear epitope-specific and complement and leukocyte-independent. The mechanisms responsible for the progression of renal disease to glomerular sclerosis have been extensively explored in the last years. Among the hemodynamic factors intraglomerular hypertension has been established to play an important part, at least in some models. (ABSTRACT TRUNCATED AT 250 WORDS)

22/3,AB/18 (Item 4 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
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06965018 89267018

Modulation of immunity in patients with autoimmune disease and cancer
treated by extracorporeal immunoadsorption with PROSORBA columns.

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IMRE Corp., Seattle, WA 98109.

Semin Hematol (UNITED STATES) Apr 1989, 26 (2 Suppl 1) p31-41, ISSN
0037-1963 Journal Code: UN9

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

Extensive animal studies and clinical observations support an immunosuppressive role for certain *antibodies* and circulating *immune* *complexes* (CIC) in malignant and autoimmune diseases. Investigators have attempted to correct or modulate dysfunction by removal of *antibodies* or CIC from plasma. Extra-corporeal immunoadsorption of plasma over columns containing a silica matrix and covalently attached highly purified staphylococcal protein A (PROSORBA column) is a procedure that specifically removes those plasma components by the interaction of protein A with the Fc region of IgG. The interaction of CIC with the Fc receptor on protein A has three specific results. First, there is direct removal of immunosuppressive CIC from the circulation. Studies of CIC-mediated immunosuppression in experimental systems have shown dose-response relationships over wide ranges of CIC concentrations. Thus, removal of CIC relative to the IgG *antibody* may be expected to exert some stimulation of the immune system. Second, the complement system is activated. Elevated levels of C3a, C4a, and *C5a* are observed in patients' circulating plasma after PROSORBA *treatment*. These levels peak one to three hours post-perfusion and are near normal levels by six hours post-perfusion. These complement components are stimulators of growth and activity of immune cells. In addition, by binding to CIC they stimulate clearance of CIC by the reticuloendothelial system. Thus, *treatments* may induce removal of more CIC than could be anticipated by the binding capacity of *treatment* columns. Third, *antibody* is released from CIC. Interaction of CIC with bound protein A with or without the aid of activated complement components leads to liberation of free *antibody*. Depending upon other factors, eg, amount of circulating antigen and/or unbound IgG, either free *antibody* or CIC containing more *antibody* relative to antigen (or both) may be infused into patients with the posttreatment plasma. Such CIC function as immune stimulators rather than suppressors of immune cell activity. The consequences of the *treatments* are summarized as follows. Stimulation of immune cellular activity is seen one to three hours posttreatment. During the first one to three *treatments*, cells of the granulocyte/macrophage series show the greatest increase. During and after *treatments* 2 to 4, lymphocytes show the greatest increase. At this point, increased blastogenic response to mitogens is observed along with an increase in the T helper/suppressor cell ratio. (ABSTRACT TRUNCATED AT 400 WORDS)

22/3,AB/19 (Item 5 from file: 154)
DIALOG(R)File 154:MEDLINE(R)
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06576106 888221106

Pathogenesis of membranous nephropathy.

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Department of Medicine, University of Washington, Seattle.

Annu Rev Med (UNITED STATES) 1988, 39 p517-30, ISSN 0066-4219

Journal Code: 6DR

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

Membranous nephropathy is the most common cause of idiopathic nephrotic syndrome in adults. Recent studies of the pathogenesis of the subepithelial glomerular immune deposits that characterize this disease have revealed new mechanisms of glomerular immune deposit formation involving cell surface antigens and have documented the role of the *C5b*-9 membrane attack complex of complement in mediating renal injury. Understanding these mechanisms may help us understand the pathogenesis of several other immune-mediated diseases and has implications for possible *therapeutic* interventions in MN.

22/3,AB/20 (Item 1 from file: 351)

DIALOG(R)File 351:DERWENT WPI

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008818741 WPI Acc No: 91-322754/44

XRAM Acc No: C91-139652

XRPX Acc No: N91-247257

Cytologic diagnosis of *immuno*-complex *glomerulonephritis* - involves *treating* kidney tissue sample obtd. by biopsy with specified *antibodies* and use of disintegration of membranes as indicator

Patent Assignee: (AMPA=) A MED PAEDIATRICS

Author (Inventor): SAKHATOV M Y A; POTAPOVA I N; IVANOV V G

Patent Family:

CC Number	Kind	Date	Week
SU 1608465	A	901123	9144 (Basic)

Priority Data (CC No Date): SU 4432219 (880525)

Abstract (Basic): SU 1608465

Immunocomplex *glomerulonephritis* is diagnosed cytologically more efficiently a sample of kidney tissue obtd. by biopsy with antidelata *antibody* and *antibody* to *C5a* fragment of the complement. The slide is then inspected under the microscope for the presence of inner complexes in the region of glomerular membranes, and the disintegration of the membranes is used as the diagnostic indicator.

USE/ADVANTAGE - Increased accuracy of diagnosis used in medicine, viz. nephrology. Bul.43/23.11.90 @(2pp Dwg.No. 0/0

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